Editorials

Risk of cancer and the oral contraceptive pill
Olav Meirik, Timothy M M Farley

New methods of analysing cost effectiveness
Andrew H Briggs

Effectiveness of chest pain units
Mike Clancy
BMJ 2007;335:623-624, doi:10.1136/bmj.39339.380093.BE

The Declaration of Helsinki
Michael D E Goodyear, Karmela Krleza-Jeric, Trudo Lemmens
BMJ 2007;335:624-625, doi:10.1136/bmj.39339.610000.BE

Physician assisted death in vulnerable populations
Timothy E Quill
BMJ 2007;335:625-626, doi:10.1136/bmj.39336.629271.BE

Letters

This week's letters

Adult coeliac disease: Rheumatic presentations are common
Alastair L Hepburn
BMJ 2007;335:627, doi:10.1136/bmj.39346.499005.3A

Value of video clips: Mobile phone videos could help treat sick children
Andrew J Ashworth
BMJ 2007;335:627, doi:10.1136/bmj.39346.512523.3A

PRP for GPs: Summary of responses
Birte Twisselmann
BMJ 2007;335:627-628, doi:10.1136/bmj.39346.699907.BE
Darzi review of health care: None so blind
Martyn C Wake
BMJ 2007;335:628, doi:10.1136/bmj.39346.513808.3A

Health equity for all: Ignorance isn't always bliss
Hugh van't Hoff
BMJ 2007;335:628, doi:10.1136/bmj.39346.489583.3A

Health equity for all: Capitalism is a force for good
Bruce G Charlton
BMJ 2007;335:628-629, doi:10.1136/bmj.39346.509699.3A

The Gillberg affair: Profound ethical issues were smoothed over
Aubrey Blumsohn
BMJ 2007;335:629, doi:10.1136/bmj.39344.519201.BE

Asylum seekers' health rights: BMA is in denial
Peter L Hall
BMJ 2007;335:629, doi:10.1136/bmj.39346.502141.3A

Asylum seekers' health rights: BMA's reply
Julian C Sheather
BMJ 2007;335:630, doi:10.1136/bmj.39346.492257.3A

Sick doctors: Uniquely disadvantaged
Anthony E Livesey
BMJ 2007;335:630, doi:10.1136/bmj.39339.569549.BE

Banning smoking: Confessions of an accordion cleaner
John F Garvey, Paul McElwaine, Thomas S Monaghan, Walter T McNicholas
BMJ 2007;335:630, doi:10.1136/bmj.39346.507778.3A

Prime minister promises a more personal NHS
Zosia Kmietowicz
BMJ 2007;335:631, doi:10.1136/bmj.39350.363553.4E

Annual check-ups aren't needed, US study says
Janice Hopkins Tanne
BMJ 2007;335:631, doi:10.1136/bmj.39349.383194.DB

Ten per cent of English girls have HPV by age of 16, survey shows
Owen Dyer
BMJ 2007;335:632, doi:10.1136/bmj.39349.571331.68

Health service needs to engage more with patients, says Nuffield Trust
Zosia Kmietowicz
BMJ 2007;335:632-633, doi:10.1136/bmj.39348.850880.BE

Doctors rank myocardial infarction as most "prestigious" disease and fibromyalgia as least
Roger Dobson
BMJ 2007;335:632, doi:10.1136/bmj.39349.486493.47

Doctors get advice on rights of children and young people
Zosia Kmietowicz
BMJ 2007;335:633, doi:10.1136/bmj.39349.377488.DB
Advice to pregnant women to avoid eating peanuts should be withdrawn, says Lords committee
Zosia Kmielowicz
BMJ 2007;335:633, doi:10.1136/bmj.39348.851968.BE

German media describe allocation of organs to Saudi patients as unfair
Annette Tuffs
BMJ 2007;335:634, doi:10.1136/bmj.39349.347801.DB

UK hip fracture audit is launched to improve care and reduce costs
Susan Mayor
BMJ 2007;335:634-635, doi:10.1136/bmj.39350.405324.DB

UK considers moving to system of presumed consent to transplantation
Clare Dyer
BMJ 2007;335:634-635, doi:10.1136/bmj.39349.483438.DB

Enter the circle, invites Nobel prize winning poet
Lynn Eaton
BMJ 2007;335:635, doi:10.1136/bmj.39349.705394.68

Better access to drugs could save 10 million lives a year, says UN expert
John Zarocostas
BMJ 2007;335:635, doi:10.1136/bmj.39349.706782.DB

In brief
BMJ 2007;335:636, doi:10.1136/bmj.39349.473785.68

Doctors should speak out on climate change, expert says
Bob Roehr
BMJ 2007;335:636, doi:10.1136/bmj.39349.474502.DB

Hillary Clinton unveils plan for healthcare reform
Fred Charatan
BMJ 2007;335:637, doi:10.1136/bmj.39346.461597.DB

Children’s health insurance in jeopardy as US Congress battles Bush
New York
BMJ 2007;335:637, doi:10.1136/bmj.39349.400069.DB

Healthcare giant advertises to children in classrooms
Ray Moynihan
BMJ 2007;335:637, doi:10.1136/bmj.39349.412326.DB

Aid agencies launch appeal for Iraqi refugees, while cholera spreads in northern Iraq
Owen Dyer
BMJ 2007;335:637, doi:10.1136/bmj.39349.436898.DB

Shortcuts from other journals: Nightly dialysis looks a promising alternative for haemodialysis patients
BMJ 2007;335:638, doi:10.1136/bmj.39346.445625.BE
Shortcuts from other journals: Global child mortality is falling too slowly
BMJ 2007;335:638, doi:10.1136/bmj.335.7621.638-a

Shortcuts from other journals: Exercise is an important treatment for type 2 diabetes
BMJ 2007;335:638, doi:10.1136/bmj.335.7621.638-b

Shortcuts from other journals: Women taking teratogenic drugs need contraceptive advice
BMJ 2007;335:638-639, doi:10.1136/bmj.335.7621.638-c

Shortcuts from other journals: US doctors must become the voice of the poor
BMJ 2007;335:639, doi:10.1136/bmj.335.7621.639

Shortcuts from other journals: Triglycerides have an independent effect on risk of heart disease
BMJ 2007;335:639, doi:10.1136/bmj.335.7621.639-a

Shortcuts from other journals: Mosquito nets reduce child deaths in Kenya
BMJ 2007;335:639, doi:10.1136/bmj.335.7621.639-b

Shortcuts from other journals: Worries remain over safety of repeated antenatal steroids
BMJ 2007;335:639, doi:10.1136/bmj.335.7621.639-c

Feature

Maternity services: How far is too far?
Adrian O'Dowd
BMJ 2007;335:640-641, doi:10.1136/bmj.39344.638623.AD

Head to head: Is there enough evidence to judge midwife led units safe? Yes
Lesley Page
BMJ 2007;335:642, doi:10.1136/bmj.39343.471227.AD

Head to head: Do we have enough evidence to judge midwife led maternity units safe? No
James Drife
BMJ 2007;335:643, doi:10.1136/bmj.39343.461146.AD

Observations

Medicine and the media: Who are the doctor bloggers and what do they want?
Rebecca Coombes
BMJ 2007;335:644-645, doi:10.1136/bmj.39349.478148.59
**Analysis**

**Use of process measures to monitor the quality of clinical practice**
Richard J Lilford, Celia A Brown, Jon Nicholl
BMJ 2007;335:648-650, doi:10.1136/bmj.39317.641296.AD

**Research**

**Cancer risk among users of oral contraceptives: cohort data from the Royal College of General Practitioner's oral contraception study**
Philip C Hannaford, Sivasubramaniam Selvaraj, Alison M Elliott, Valerie Angus, Lisa Iversen, Amanda J Lee

**Preventive strategies for group B streptococcal and other bacterial infections in early infancy: cost effectiveness and value of information analyses**
Tim E Colbourn, Christian Asseburg, Laura Bojke, Zoe Philips, Nicky J Welton, Karl Claxton, A E Ades, Ruth E Gilbert

**Effectiveness and safety of chest pain assessment to prevent emergency admissions: ESCAPE cluster randomised trial**
Steve Goodacre, Elizabeth Cross, Cath Lewis, Jon Nicholl, Simon Capewell, ESCAPE Research Team
[extra: The ESCAPE Chest Pain Unit] [extra: ESCAPE Chest Pain Unit data collection form]

**Clinical review**

**Managing anovulatory infertility and polycystic ovary syndrome**
Adam H Balen, Anthony J Rutherford
BMJ 2007;335:663-666, doi:10.1136/bmj.39335.462303.80

**Practice**

**Guidelines: Care of healthy women and their babies during childbirth: summary of NICE guidance**
Sara Kenyon, Roz Ullman, Rintaro Mori, Martin Whittle
BMJ 2007;335:667-668, doi:10.1136/bmj.39322.703380.AD
**Patients with cardiac chest pain should call emergency services**
Will T Roberts, Adam D Timmis
BMJ 2007;335:669, doi:10.1136/bmj.39342.693252.47

**Views & reviews**

**Personal view:** Ethicist on the ward round
Daniel K Sokol
BMJ 2007;335:670, doi:10.1136/bmj.39344.636076.59

**Review of the week:** The alcohol industry: taking on the public health critics
Michael Farrell
BMJ 2007;335:671, doi:10.1136/bmj.39337.431667.4E

**From the frontline:** Running with the pantomime horses
Des Spence
BMJ 2007;335:672, doi:10.1136/bmj.39349.463148.47

**The best medicine:** A different perspective
Liam Farell
BMJ 2007;335:672, doi:10.1136/bmj.39349.471470.47

**Between the lines:** Doctor-anarchists in class war
Theodore Dalrymple
BMJ 2007;335:673, doi:10.1136/bmj.39344.549931.59

**Medical classics:** Cancer Ward
Paul Crichton
BMJ 2007;335:673, doi:10.1136/bmj.39329.524942.34

**Obituaries**

**This week's obituaries**

**Bjørn Ibsen**
Caroline Richmond
BMJ 2007;335:674, doi:10.1136/bmj.39344.561250.BE

**Michael Gerald Askew**
Donald McNutt, Roz Reid
BMJ 2007;335:675, doi:10.1136/bmj.39337.683056.BE

**Nina Agnes Jane Carson**
Dennis Carson
BMJ 2007;335:675, doi:10.1136/bmj.39343.739525.BE

**Ian Patrick Mulligan**
Patrick Davey
BMJ 2007;335:675, doi:10.1136/bmj.39336.666030.BE

**Anand Mohan Sur**
Poorvaali Sur
BMJ 2007;335:675, doi:10.1136/bmj.39329.694201.BE

**David Tidmarsh**
Henry R Rollin
BMJ 2007;335:675, doi:10.1136/bmj.39343.690532.BE
Japhet Mara Urasa
Krishna Somers
BMJ 2007;335:675, doi:10.1136/bmj.39337.665868.BE

**Minerva**

**Minerva**
BMJ 2007;335:676, doi:10.1136/bmj.39345.661794.801

**Minerva**
Ruth Macpherson, Lucy Hill
BMJ 2007;335:676, doi:10.1136/bmj.39345.661794.80

**Fillers**

*BMJ updates: Bupropion helps primary care patients stop smoking*

BMJ 2007;335:662, doi:10.1136/bmj.39345.697917.AD

**Relative risk**
Stephen J Hanna
BMJ 2007;335:666, doi:10.1136/bmj.39129.623368.BE
In the preface to the first comprehensive publication from the Royal College of General Practitioners’ oral contraception study Sir Richard Doll wrote, “Final judgement on the safety of the pill must still await the passage of time, when observations can be made of women who have used the pill for 10 or 20 years.” Thirty years later, in this week’s BMJ, Hannaford and colleagues’ report incidence rates of cancer in relation to use of the pill among women in the study cohort.

Between 1968 and 1969, 45 950 women in the United Kingdom were enrolled in the study, and they were followed for a mean of 24 years. Full assessment of the risk of cancer needs a long follow-up as effects of the pill may persist many years after its use has been stopped. Incidence rates of cancer in women who ever used the pill were compared with rates in women who never used the pill. On balance, no higher risk of cancer was found in pill users. Risks were significantly lower for cancer of the colon or rectum, uterine body, or ovaries; the main gynecological cancers combined (uterine body, ovaries, cervix); and for any diagnosis of cancer. The incidence of breast cancer was similar in pill users and never users.

These data came from six monthly reports from the women’s general practitioners until 1996, and from linkage of the 35 050 women still in the study in the mid-1970s to National Health Service central registries. These provided cancer diagnoses until 2004 to supplement those reported by general practitioners. The follow-up covered two thirds of the women’s years that would have accumulated if all 45 950 women had been followed from 1968 or 1969 to 2004.

Hannaford and colleagues also report analyses restricted to follow-up by general practitioners until 1996, which allow incidence rates to be calculated according to duration of pill use and time since stopping use of the pill. The comparisons between ever users and never users were largely similar for the two sources of data. After adjustment for age, parity, smoking, social class, and use of hormone replacement therapy, the relative risks of cancers of the ovary and uterine body in ever users compared with never users were below unity for all durations of pill use (≤48, 49-96, and ≥97 months). The opposite was found for cancers of the cervix and the brain or pituitary—relative risks increased progressively with longer use. The patterns of risks by time since stopping the pill were largely reassuring, although some excess risk of cervical cancer persisted 10-15 years after stopping, and risk of brain or pituitary cancer persisted 20 or more years after stopping. Some individual risk estimates are significantly different from 1.0; for example, risk of breast cancer was increased 15-20 years after stopping, yet was significantly reduced 20 or more years after stopping. Considering the many comparisons included in the paper, individual risk estimates must be interpreted with caution.

The data from this and other studies indicate that pill use prevents or postpones ovarian and endometrial cancers but probably accelerates development of cervical cancer caused by chronic infection with oncogenic human papillomavirus. Fortunately, preinvasive cervical cancer can be detected by cervical cytology and treated. Regular cervical cytology screening remains an important element of quality health care, particularly for women who use the pill.

The finding that pill use increases the risk of brain or pituitary cancers may result from prescription bias—menstrual disturbances are often regulated by the pill, and such disturbances may be an early symptom of pituitary disease. One study of pituitary prolactinomas and pill use found odds ratios of 7.7 (95% confidence interval 3.5 to 17.0) in women prescribed the pill for treatment of menstrual irregularities and 1.3 (0.7 to 2.6) in women prescribed the pill for contraception.

Considering that the Royal College of General Practitioners’ study enrolled women almost 40 years ago, the age distribution of pill users is remarkably similar to current patterns of use. At enrolment, 61% of pill users were under 30 years, and the age group 20-24 years had the largest number of women. A UK survey in 2005-6 showed that 52% of pill users were under 30 and the highest prevalence of pill use was among 20-24 year olds.

Pills used in the late 1960s and 1970s contained higher dosages of progestogens and oestrogen (ethinylestradiol) than the currently widely used 30 µg ethinylestradiol combined pills. Pill users in the study would have started with higher dose pills, with a progressive switch to the lower dose formulations used today. Limited data suggest that the reduced risks of ovarian and endometrial cancers are maintained with lower dose pills, so that the overall balance of cancer risks can be expected to apply to today’s pill users.
The results of this unique long term study agree with findings from the Oxford Family Planning Association’s cohort study and modelling studies.4,5 The results show that—in a developed country with an effective cervical cancer screening programme—the pill is a safe contraceptive method with respect to cancer. In some developing countries—with inadequate cervical cancer screening and healthcare services, and high cervical cancer rates—the balance of cancer risk is probably less favourable.6 However, in such settings, contraceptive benefits must be weighed against the risk of cervical cancer, and the balance would tilt in favour of the pill because of the high morbidity and mortality associated with unplanned pregnancies.

New methods of analysing cost effectiveness

Value of information analyses must be integrated into the process of commissioning primary research

Interest in whether health interventions are value for money as well as effective has meant that the term cost effectiveness7 is commonly used (and sometimes misused) in the clinical literature. Consequently, methods for determining cost effectiveness have been refined, especially techniques for synthesising evidence and representing uncertainty in the results of such evaluations. Techniques such as multi-parameter evidence synthesis8 and value of information analysis9 are now routinely integrated into cost effectiveness studies, especially health technology appraisals (HTAs) conducted for the National Institute for Health and Clinical Excellence. But is there real value in the development and application of such techniques, or have these new methods emerged simply as a consequence of involving academics in the process of evaluation?

In this week’s BMJ, Colbourn and colleagues present a cost effectiveness and value of information analysis of strategies for preventing group B streptococcal and other bacterial infections in early infancy.10 This is a timely assessment of the potential cost effectiveness of various ways of organising a national screening programme for group B streptococci, which can influence UK policy on whether (and how) to implement such a screening programme. However, what do the sophisticated techniques used add to what we already know about the effectiveness and cost effectiveness of preventive strategies for this infection?

Firstly, the techniques of decision analysis combined with multi-parameter evidence synthesis allow a comprehensive assessment of all of the evidence that relates to the policy question, including the consideration of all possible strategies (something Colbourn and colleagues have taken to the extreme, with 341 strategies evaluated in this paper alone). This contrasts with the Cochrane review approach, which typically uses only randomised evidence to assess a single treatment comparison.

In addition, a probabilistic analysis of uncertainty in the parameters of the model allows a full assessment of the implication of the estimated uncertainty for the decision. This means the analysis can answer two fundamental questions relating to the choice between the strategies evaluated. Firstly, on the basis of the existing evidence, what is the preferred course of action? Secondly, should additional information be collected to better inform that decision?

The analysis by Colbourn and colleagues shows that, on the basis of existing evidence, it is likely that immediate changes to the organisation and delivery of services to prevent group B streptococcal infection would greatly benefit the health service. Furthermore, given the size of the population concerned, it highlights the value of further research, particularly into the potential use of an intervention (vaccination) that is not yet available in the United Kingdom. However, as the authors point out, even though further research may be valuable this does not mean that the proposed trial of screening for group B streptococci, at an estimated cost of £12m (€18m; $24m), is the correct way forward. Indeed, the analysis suggests that the screening strategies proposed as comparators in this trial are unlikely to be cost effective.

In the absence of an available vaccine, the value of additional evidence currently lies elsewhere—particularly in resolving the choice between intravenous and oral drugs for certain preterm infants. It is unfortunate that the two teams responsible for the synthesis of evidence11 and the design of a clinical trial, both funded by the HTA programme, seem to have worked independently and concurrently. The value
Effectiveness of chest pain units

Trial shows no benefit overall, but success may vary as a result of operational factors that are difficult to measure

Acute chest pain is responsible for one in four emergency medical admissions in the United Kingdom, and these figures are probably similar in most Western countries. People with chest pain are rightly encouraged to seek help early, and attendances to emergency departments are rising. Emergency departments are responsible for quickly identifying and treating people with acute myocardial infarction and unstable angina, and for evaluating people with a lower likelihood of acute coronary syndrome.

Identifying which patients at low risk of acute coronary syndrome can be safely sent home and which patients need further observation and investigation is not easy, especially when the consequences of misdiagnosis include infarction, arrhythmia, and death. The strategy of evaluating such patients in a chest pain unit based within or near the emergency department is used in 30% of emergency departments in the United States. The practice is supported by randomised trials that studied particular risk groups and methods of diagnosis, and in healthcare settings specific to the US, so the results may not be generalisable elsewhere. In theory, a chest pain unit should improve outcomes—but does it?

In this week’s BMJ, a cluster randomised controlled trial (effectiveness and safety of chest pain assessment to prevent emergency admissions; ESCAPE) by Goodacre and colleagues tries to answer this question. It follows on from the encouraging results of a previously reported single centre randomised trial, which found that a chest pain unit reduced hospital admissions and health service costs.

The ESCAPE trial enrolled 14 hospitals, seven of which had a chest pain unit. The trial defined low risk patients as those with chest pain possibly as a result of acute coronary syndrome, but who had no new electrocardiographic changes diagnostic of the syndrome or prolonged or recurrent cardiac-type pain. In people admitted to hospitals with a chest pain unit, serial electrocardiography was performed over two to six hours, biochemical markers were measured, and an exercise treadmill test was typically performed the next working day. People admitted to hospitals without a chest pain unit received the usual service typically consisting of admission for troponin measurements over 12 hours, with no early exercise testing. The outcomes were measured the year before and the year after either the introduction of the chest pain unit or continuation of the same service. The introduction of a chest pain unit had no significant effect on the proportion of people attending the emergency department with chest pain, the proportion of people with chest pain who were admitted, or the number of people admitted over the next 30 days. However, a small increase was seen in the proportion of patients readmitting (odds ratio 1.10, 95% confidence interval 1.00 to 1.21, P=0.036) and in the number of daily medical admissions (1.7 per day, 0.8 to 2.5, P<0.001).

Setting up a chest pain unit led to more patients being tested, but no reduction in the proportion of patients admitted. Why was this? Perhaps different staffing levels and opening hours reduced the impact of the chest pain unit—this might partially explain the variation in the proportion of adult attendances managed in these units (1-7/1000 attendances at the emergency department). The variation in the average age, risk factors, and known coronary heart disease between the chest pain units suggests that some patient selection occurred. Why was there no effect overall even though some chest pain units worked well? Perhaps factors that determine the success of a service (such as enthusiasm of the staff, buy in by other relevant specialties) are difficult to measure in a trial setting. Clearly, one size does not fit all, and how

these services fit within the wider context of health care is important.

Patients expect serious disease not to be missed, and unless hospitals are explicit about what risks they are prepared to accept and pay for, clinicians will use whatever tests and periods of observation they can to rule out serious disease. The failure of this trial to show a benefit of chest pain units does not reduce the need to find and implement a diagnostic strategy to discriminate in this growing low risk patient population between patients with a low likelihood of an adverse outcome related to the acute coronary syndrome—who can be safely discharged—and those who need further treatment or inpatient evaluation. Future studies need to focus on the successful implementation of a new diagnostic service and where possible how such testing can be simplified.

The Declaration of Helsinki
Mosaic tablet, dynamic document, or dinosaur?

The Declaration of Helsinki is a respected institution and one of the most influential documents in research ethics. Having withstood five revisions and two clarifications since its conception in 1964. Its guardian, the World Medical Association, recently invited submissions for further revision.

The history of the declaration has been well documented. The Nuremberg Code (1947) was one of the first statements of the ethical principles involved in human experimentation. However, because of its association with Nazi war crimes it had relatively little effect on practice. The Declaration of Helsinki dealt with clinical research more directly, but was portrayed as a weakening of the stringent protections of Nuremberg. Nevertheless, for a quarter of a century only minor changes were made and it became engrained in the international culture of research ethics.

In 1996, the declaration added a reference to placebos in response to concerns about trials in perinatal HIV transmission in developing countries. Critics pointed out that continuing to use placebos when efficacy had been demonstrated implied a different ethical standard for developing countries than for developed ones. Having entered into the specifics of trial design the declaration was drawn into a debate on whether ethical principles are universal or are relative to the context in which they are applied and also into related principles of research in developing countries.

The World Medical Association was then pressured to make more radical reforms. An American proposal, seen by some as a further attempt to weaken the declaration, resulted in a vigorous debate, but despite lack of consensus and strong feelings by some that it should not be changed, a major revision was approved in 2000. This did little to improve acceptance.

Concerns were also expressed that the cumulative changes represented a shift towards protecting the efficacy of research at the expense of the protection of human subjects. A division between developed and developing countries also emerged with claims of American ethical imperialism. Although new emphasis on social justice and a duty to benefit communities as well as individuals received praise. Complaints about clarity resulted in the addition of footnotes in 2002 and 2004, but this also failed to achieve global endorsement. The situation was further complicated by the appearance of other guidelines, including those from the Council for International Organizations of Medical Sciences, the Nuffield Council, and Unesco (United Nations Educational, Scientific, and Cultural Organisation), which were seen to be potentially conflicting. It was even suggested that the declaration was out of touch and irrelevant.

The debate on the future of the declaration raises several fundamental questions about the essential purpose of the declaration, its structure (basic principles or procedural rules), its status (static or dynamic), the extent to which it can influence understanding and practice, and the nature and limits of universality in ethics.

The nature of the declaration has progressively changed from simply restating Nuremberg as an ethical code to being increasingly prescriptive. The more procedural basis it has become the more divergent opinion has become, with calls for reversion to the simplicity and conciseness of a Nuremberg-like document. Other guidelines by contrast provide detailed commentaries, and the declaration may fail by being neither code nor commentary. The arguments surrounding the declaration point to a failure to clearly separate related but distinct concepts—standard of care, ethical standards, ethical principles, and the operationalisation of principles.

Whether “ethical standards” are considered universal will depend on what exactly is meant by this term. They have been criticised as representing the North

Physician assisted death in vulnerable populations

Claims of increased risk in these groups are not supported by evidence

Physician assisted death (both voluntary active euthanasia and physician assisted suicide) has been openly practised in the Netherlands for more than 25 years and formally legalised since 2002. The practice has been analysed in four major national studies between 1990 and 2007. A more restricted form of physician assisted death (physician assisted suicide only) was legalised in Oregon in 1997 and is the subject of an annual report (www.oregon.gov/DHS/ph/pas/index.shtml). Although these studies do little to resolve the moral and religious questions surrounding these practices, they do answer the following questions about the risks and benefits of legalisation.

Will these practices become more common over time in a permissive environment? In Oregon, physician assisted death accounts for around one in 1000 deaths each year, with no significant change in frequency over nine years. All patients have met the necessary criteria, and more than 85% were also enrolled in hospice programmes. In Oregon, one in 50 dying patients talk to their doctors about assisted death and one in six talk to family members. There seems to be much conversation about end of life options, therefore, but relatively few cases of assisted death. Oregon is among the nation’s leaders in other markers of good end of life care, including deaths at home, opioid prescribing, hospice enrolment, and public awareness about end of life options. The Dutch practices of physician assisted death have also remained stable over the duration of four studies.
and hospice and palliative care have become more prevalent in recent years.

Will the burdens and risks of these practices fall disproportionately on vulnerable populations? A study by Battin and colleagues published in this week’s *Journal of Medical Ethics* that analyses existing databases from Oregon and the Netherlands dispels many of these concerns. They found no increased incidence of physician assisted death in elderly people, women, people with low socioeconomic status, minors, people in racial and ethnic minorities, and people with physical disabilities or mental illness. The one exception was people with AIDS, and studies from San Francisco completed before protease inhibitors were used also showed a high prevalence of physician assisted death in this population. These findings call into question the claim that the risks associated with legalisation will fall most heavily on potentially vulnerable populations.

Are data available about these practices in places where physician assisted death is prohibited? Our study in 1998 assessed the secret practice of assisted death (both physician assisted suicide and voluntary active euthanasia) in the United States, and found significantly higher rates (about one in 50 deaths) than in Oregon after legalisation. The data are not directly comparable, as the study strategy we used safeguarded the surveyed doctors to ensure anonymity (similar techniques are used to study other illegal practices). This may have meant that the participating doctors were less representative and that they reported their practice differently than if the practice were legal. None the less, it raises the possibility that legalisation and regulation with safeguards may protect rather than facilitate the practice.

Are there some cases in legal environments that do not meet the criteria and are not reported? The most controversial cases in the Netherlands are the life ending acts that have no explicit requests (known as LAWER cases – with about 1000 cases each year). Most, but not all, of these patients were suffering greatly and had lost the ability to make decisions for themselves, and many had previously given consent for physician assisted death under such circumstances. The number of such cases, has decreased over time, but they still account for about 0.4% of deaths that fall outside the Dutch guidelines on voluntariness. It is tempting to attribute such cases to legalisation becoming a slippery slope, but a recent study of six Western European countries – using the same format and questions as the Dutch studies – showed that four of the six countries where assisted death is illegal had a much higher incidence of LAWER cases than is seen in the Netherlands. In fact, such cases were more common than cases of assisted death where voluntary consent was given (either voluntary active euthanasia or physician assisted suicide).

What happens in the US to patients without mental capacity who are dying and whose suffering cannot be relieved by usual palliative measures? Evidence based answers to this question are unknown, but there is likely to be extreme variability in the face of the legal and moral uncertainty about responsibilities, risks, and acceptable approaches. Clinical experience suggests that we deal with many of these patients using terminal sedation, a last resort that has been legal in the US since the 1997 US Supreme Court ruling. No formal tracking is available for this practice in Oregon or elsewhere in the US. Limited data suggest that the practice of terminal sedation is highly variable and accounts for 0-44% of deaths, depending on definitions and programmes. In the Netherlands, terminal sedation accounted for 5.6% of deaths in 2001, compared with 7.1% in 2005 (it was not measured in the first two studies). Many patients who receive terminal sedation are actively dying, experiencing severe physical suffering, and have lost capacity, so some were probably categorised as LAWER cases in previous Dutch studies. Terminal sedation is a legal practice in the US that could be improved if directed by carefully crafted guidelines and reporting.

These days, patients who are dying are faced with a wide array of uncertainties and choices, and the physical and psychological challenges they experience are more complex. Available data suggest the risks and benefits of controversial practices like physician assisted death or terminal sedation are more favourable when practitioners work together with patients and families in an open and accountable environment. Secret practices and arbitrary restrictions should be avoided whenever possible.

Studies such as those by Battin and colleagues from Oregon and the Netherlands help clarify the actual risks and benefits of legalisation of physician assisted death to vulnerable populations. We should ensure that pseudo-scientific arguments are not used to promote particular moral values and associated restrictions. Patients who are dying and their families need us to be as objective and honest as possible in these deliberations.
We select the letters for these pages from the rapid responses posted on bmj.com favouring those received within five days of publication of the article to which they refer. Letters are thus an early selection of rapid responses on a particular topic. Readers should consult the website for the full list of responses and any authors' replies, which usually arrive after our selection.

ADULT COELIAC DISEASE

Rheumatic presentations are common

Hopper et al highlight the non-specific way in which coeliac disease can present in adults.1 Presentations to rheumatology services are not uncommon with symptoms including fatigue, weakness, non-specific arthralgia, muscle cramps, and myalgia. A good argument therefore exists for screening for this disease when patients present with what may seem initially to be fibromyalgia or chronic fatigue syndrome (CFS), using combined serological testing. Such screening for coeliac disease is included in the recently published NICE guidance on the management of CFS.2 A true arthritis has also long been recognised.3 1 Presentation in elderly people is rare but also described and deserves mentioning.4

A gluten-free diet is the mainstay of treatment of the metabolic bone disease that may complicate coeliac disease. A mixture picture of osteomalacia and osteoporosis may be seen, and vitamin D replacement may have an additional role to improve both symptoms and to reduce the risk of fracture. A low serum measurement of vitamin D may be the only abnormality found on biochemical testing, and screening should be considered in patients with premenopausal and male osteoporosis. Presentation with mixed deficiency anaemia is also possible, rather than iron deficiency alone, a low serum concentration of folate in particular being a fairly sensitive early indicator of the disease. Finally, coeliac disease may develop in patients with primary autoimmune rheumatic disease such as systemic lupus erythematosus and Sjogren's syndrome, and vice versa.

Occasionally non-specific musculoskeletal presentations may lead to the erroneous prescribing of corticosteroids. This may lead to false negatives on subsequent duodenal biopsy. However, corticosteroids may improve both gastrointestinal and musculoskeletal symptoms, and may be used to treat refractory disease. Other forms of immunosuppression—such as azathioprine and infliximab—are also used in refractory cases.5

Alastair L Hepburn consultant rheumatologist Worthing Hospital, Worthing BN11 2DH alinhepburn@doctors.org.uk

Competing interests: None declared.

1 Hopper AD, Hadjivassiliou M, Butt, S, Sanders DS. Adult coeliac disease. BMJ 2007;335:558-62. (15 September)

VALUE OF VIDEO CLIPS

Mobile phone videos could help treat sick children

Cutting argues that screen images of sick children are good enough to train those who have to assess sick children.1 Most parents (even the most socially deprived) now have access to mobile phones with video recording facilities that may be transmitted immediately through the mobile phone network. If screen images are good enough for teaching, they may be good enough to aid assessment.

Centralised or out of hours services could easily and inexpensively be enhanced to permit parents to transmit video images of sick children for assessment by a suitably trained clinician.

Modern technology in the form of video clips should play a part not only in training but also in treatment.

Andrew J Ashworth general practitioner principal Davidsons Mains Medical Centre, Edinburgh EH4 5B Andrew.ashworth@lothian.scot.nhs.uk

Competing interests: None declared.

1 Cutting WAM. Video clip is worth 1000 words. BMJ 2007;335:527. (15 September.)

PRP FOR GPS

Summary of responses

The editorial by cardiologist David S Wald on performance related pay (PRP) in primary care sparked 12 responses, mostly from aggrieved UK general practitioners (GPs).1 2 United in their opposition to Wald’s suggestions for a “revised” quality and outcomes framework (QOF), several of the respondents point out that a hospital consultant may not be best placed to write about issues affecting primary care and the increasing complexity of primary care consultations.

Many are compelled to clarify that the QOF payments are not incentives for the GPs themselves. There may not be enough awareness of the changed ways of working and workloads that GPs have adopted, which, combined with their achievements in implementing new systems and targets, may justify a different system of pay and incentives. And measuring risk factors is only a part of preventive measures, not an end in itself.

Andrew Wijnberg, a GP in Birmingham, takes issue with Wald’s comparison: “It is not fair to compare the QOF with paying police to catch criminals or firemen incentives to put out fires; the payments for performance are more akin to a performance pay for the police or fire organisation in achieving national standards in detection rates and prevention.”

One way out of GPs having to justify themselves every step of the way might be “to ask the public what it wants from their GPs and then pay GPs to provide it,” writes Ian Quigley, a GP from Romford. And in the only letter from outside the UK, academics Joachim Sturmberg and
DARZI REVIEW OF HEALTH CARE

None so blind

Heath puts forward some solid arguments against the polyclinic concept proposed in Lord Darzi’s review of health care in London, but she is blind to the deficiencies in our services, cited in A Framework for Action.²

In some places, access to general practitioners’ services, even by telephone, is inadequate. Some practices still close for half a day each week or are not open throughout the day. The problem of poor access and availability is perceived by public and politicians as unacceptable in a service that has received so much investment in recent years and as major contributors to the rise in emergency activity and attendance at hospital accident and emergency departments. Pressure is mounting on us to increase our hours of routine availability.

Polyclinics will not solve all these problems, but they will facilitate groupings of clinicians sufficient to offer extended hours and types of care and to act as the front door to accident and emergency care in some locations. Over 50% of people attending accident and emergency departments would receive better care from primary care practitioners rather than being seen by junior doctors, over-investigated, and even admitted to hospital.

Ignorance isn’t always bliss

I am struck by the global absence of a debate about health literacy in achieving health equity for all¹. Patients (users) in all countries have a right to information about health. This is enshrined in the constitution of the World Health Organization of 1946. If we are to share our knowledge we need to share a common language. Up to now advocates of health literacy have suggested we remove technical language—a sort of dumbing down.

I propose that we give up our hold on medical information and make it available to all from primary school on—this would entail a massive effort by government, medics, and educationalists to re-package the information, but it’s worth looking at. By doing this we would be educating children about the social, political, geographical, and “medical” (infectious, degenerative, etc) causes of disease, and we would be altering presently dry subject areas such as history, geography, and statistics. Furthermore, we would be emancipating children to make their own decisions and possibly helping with the downturn in interest in pure sciences in the developed nations.

I have started an educational pilot programme (www.facts4life.org) along these lines in my local secondary school and will soon start direct patient education in my surgery. The aim with both is for clients to understand the processes involved in illness and by doing so reach a more rounded view about their problem and be better able to own their condition and take more responsibility for it. This doesn’t mean we are trying to teach them that the doctor is always right—more that the science on which we make decisions is valid if sometimes poorly used.

Capitalism is a force for good

Maryon-Davis’s editorial embodies the doctrinaire anticapitalism characteristic of public health administrators, including the World Health Organization.¹ This bias leads to stunning misrepresentations of reality and currently stands as a major obstacle to improving world health.

The largest scale reduction of poverty in the history of the planet has occurred over the past two decades. This unprecedented progress is mainly due to the progressive adoption of capitalism by the vast populations of China, India, and other Asian nations: China alone is lifting a million people a month out of poverty.² Yet Maryon-Davis seems not to have noticed this.

The poorest parts of the world are the least capitalist. Some nations in sub-Saharan Africa are going backwards. In Malawi the standard of living (daily calorie consumption) is perhaps the lowest that has ever existed in human history. This is a consequence of medical advances which allow population to increase even during chronic famine.³

Poverty is bad for health; and wealth is the only thing that can cure poverty.¹ And China and India show that capitalist wealth creation is effective, while the more “socialist” and redistributive WHO strategy (focusing on health equity) has a poor track record.

The entrenched ideology of anti-
modernisation among international public health professionals stands in the path of further progress, both at home and abroad. What the sick and poor of the world need is more capitalism, more industrialisation, and more globalisation.

Bruce G Charlton editor-in-chief, Medical Hypotheses University of Newcastle on Tyne, Newcastle on Tyne NE1 7RU bruce.charlton@ncl.ac.uk

Competing interests: None declared.

1 Maryon-Davis A. Achieving health equity for all. BMJ 2007;335:522-3. (15 September.)

THE GILLBERG AFFAIR

Profound ethical issues were smoothed over

The issue at the heart of the Gillberg affair concerns the relation between raw data and the representation of those data. That issue is central to most recent scandals that have damaged the scientific basis of medicine and the trust of patients. It also concerns the availability of raw data to journals, fellow scientists, consumers, those who claim to police matters of integrity in science, and even to authors themselves. In short, it concerns the safety of the entire scientific enterprise.

Gornall’s article skirts around every one of the principles while making conjectures about the personalities involved. The only fact of the affair that is relevant to a serious discussion of ethics is straightforward. The Gillberg team destroyed raw data, having faced an accusation of research misconduct pertaining to those data. They destroyed those data despite a court order that the data should be made available for scrutiny.

The argument about confidentiality is entirely spurious and could be made about practically every bit of clinical research that has ever been carried out. Is it really being suggested that no one (regulatory bodies, courts, bodies investigating research misconduct, trial participants themselves, coauthors, journal editors, research councils, or even authors of the science itself) should ever be allowed to scrutinise any aspect of research? This is not science, and the article that originated this discussion is not part of any form of legitimate scientific debate.

Journals such as the BMJ may request raw data from human studies when fraud is suspected, as do a variety of other bodies. There is nothing at all special about the Gillberg study that makes it an ethical outlier exempt from the usual norms of science. At least no such reason has been provided in anything I have read. In the well publicised case of Singh, which also involved the destruction of raw data (in his case termites provided the excuse), the failure to provide raw data provided grounds for suspicion of scientific misconduct—not congratulations. The apparent moral of the report by Gornall is that future researchers faced with questions about the plausibility of their findings should simply destroy their data.

Aubrey Blumsohn consultant, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield S5 7AU abulumsohn-3@yahoo.co.uk

Competing interests: None declared.


ASYLUM SEEKERS’ HEALTH RIGHTS

BMA is in denial

Despite the evidence that the 2004 charging regulations that bar access to free NHS hospital care violate refused asylum seekers’ human rights, the BMA has never acknowledged the fact. Now the government has raised the stakes immeasurably—the years of confusion, procrastination, hounding, and denial of hospital care will appear small beer if its threat to also ban access to free primary care is implemented this October, as is widely expected.

An unconscionable disconnect exists between BMA high profile support for health rights, as reflected by Mary Robinson’s prestigious launch of the BMA’s Right to Health: a Toolkit for Health Professionals, and apparent institutional resistance to incorporate health rights into policy. As the toolkit says, the right to the highest attainable standard of health is a fundamental human right, protected by international law, and the state must refrain from denying equal access for asylum seekers and illegal immigrants.

The ethics department stipulation that the membership inform BMA policy has been met by the unequivocal 1997 instruction from the annula general meeting to the BMA Council “to campaign against embargoes which damage health.” On this occasion the government imposing sanctions is British and the victims live in the UK, but the ethical issues are identical.

As the chairman of the international committee proudly explained in his ARM speech, the toolkit provides a basis by which medical associations and populations can hold their governments to account regarding the provision of health care. If the BMA continues to disregard its own educational material, it will surrender its reputation for integrity and its status as an authority on human rights. If it persists in its role as the watchdog that failed to bark, and the government withdraws free access from all health care for refused asylum seekers, the medical profession will—to the extent that its passivity has shown a green light to the government’s violation of international human rights law—share responsibility for the suffering and deaths that ensue.

Peter L Hall chair, Doctors for Human Rights Pasque Hospice, Luton LU3 1NT peterhall@doctorsforhumanrights.org

Competing interests: PLH played a part in developing the General Comment 14 of the International Covenant on Economic, Social and Cultural Rights.

5 Sheather J. BMA’s response. BMJ 2007;334:917. (5 May.)
BMA's reply

While I have sympathy with Hall's comments it is difficult to see how much further it is possible to take policy in this area. The BMA is a democratic membership organisation, and a trade union and professional organisation. It is not a campaigning human rights organisation. The momentum behind its human rights work has come from the democratic work of its members. If the government decides that it wishes to withdraw eligibility for free primary health care for failed asylum seekers, then, should they chose to do so, it is for the BMA's members, working through its regional and committee structures, to develop targeted policy. As a member of the secretariat of the BMA's ethics department I have been involved in numerous meetings with BMA members and senior government figures, trying to ensure that any legislation in this area retains a minimum of humane flexibility. I have done this in quiet pursuit of established BMA policy.

On a broader point, working with a small secretariat the ethics committee has striven for many years to draw attention to the importance of human rights in both the provision of health care and in the underlying determinants of health. This has been in addition to its core work in medical ethics. The BMA has achieved some success in this area. I would call on Hall, as a committed human rights activist, to try to support us for the work that we have been able to achieve, rather than to criticise us for what we have been unable to deliver.

Julian C Sheather senior ethics adviser
Ethics Department, BMA, BMA House, London WC1H 9JP
jcsheather@bma.org.uk

Competing interests: JCS is a senior ethics adviser at the BMA. He is the department's lead on health and human rights and a coauthor of The Right to Health: a Toolkit for Health Professionals.

SICK DOCTORS

Uniquely disadvantaged

Klitzman's article on interviewing doctors as patients highlighted interesting and important perspectives on the patient's position, role, and motivations, as well as the unique position of doctors as patients.1

Sometimes seen as a perk of the job by others, I suggest that doctors may occupy a uniquely disadvantaged position when ill.

We may struggle with taking time off work, taking up the time of an already busy colleague, and the impossibility of remaining objective about our own condition (usually underplaying symptoms). This position is further exaggerated by guilt at not having been able to manage our condition without recourse to a fellow doctor. The complicated set of dynamics can be further exaggerated if we present with a depressive illness or other psychiatric condition. Any objectivity and insight is long gone, and feelings of guilt, worthlessness, and inadequacy compound a difficult presentation but also affect the ongoing relationship needed for treatment. We may also harbour anxieties around having to maintain a professional relationship with our physician when we return to work.

As a profession I am not sure that we are sufficiently aware of (or comfortable with) the position of the sick doctor. Fearing a possible charge of nepotism should not deter us from looking closer.

Anthony E Livesey consultant in adolescent psychiatry
Oakwood Young People's Centre, Sheffield S5 7TF
anthony.livesey@sch.nhs.uk

Competing interests: None declared.

1 Klitzman R. Pleasing doctors: when it gets in the way. BMJ 2007;335:514. (8 September.)

BANNING SMOKING

Confessions of an accordion cleaner

Haw and Gruer document the reduction in exposure to secondhand smoke since the implementation of smoke-free legislation in Scotland.1 We report further evidence of reduced exposure to secondhand smoke in Irish pubs since the legislation in the Republic of Ireland.2 3

The pub session (or seisiún in Gaelic), where musicians gather to play traditional music together, is commonplace throughout bars in Ireland. Instruments include the accordion, concertina, melodeon, and Uilleann (or Irish) bagpipes, all of which are bellows driven instruments.

There is anecdotal evidence that the interiors of accordions played regularly in smoke filled environments are dirtied as a result of the trapping of contaminant particles circulating in the air as it filters through the instrument. We conducted a telephone survey of all workers involved in the cleaning, repair, maintenance, and renovation of accordions in the Republic of Ireland. We managed successfully to contact six out of seven such workers.

All participants pointed out that a strong smell of cigarette smoke emanated from accordions played in a smoke filled environment when they are opened. Soot-like dirt is also deposited throughout the instrument but particularly where air enters the bellows through the air inlet valve and on the reeds. One repairer commented that the deposition of dirt could be substantial enough to affect the pitch of the reed. Two others claimed that if a musician tended to play in a particular key, that this could be determined from the distribution of dirt around particular reeds. All who were questioned stated categorically that these signs had definitely improved in accordions they had worked on since the introduction of the smoking ban in Ireland.

Our results show that the smoking ban has improved air quality in Irish bars and its implementation in the face of initial opposition has been music to the ears of the people of Ireland.

John F Garvey specialist registrar john.garvey@ucd.ie
Paul McElwaine clinical tutor
Pulmonary and Sleep Disorders Unit, St Vincent's University Hospital, Dublin 4, Republic of Ireland
Thomas S Monaghan specialist registrar (neurology) Beaumont Hospital, Dublin 9
Walter T McInlichias director Pulmonary and Sleep Disorders Unit, St Vincent's University Hospital

Competing interests: None declared.

1 Haw SJ, Gruer L. Changes in exposure of adult non-smokers to secondhand smoke after implementation of smoke-free legislation in Scotland: national cross sectional survey. BMJ 2007;335:549. (15 September.)
Prime minister promises a more personal NHS

Zosia Kmietowicz LONDON
Prime Minister Gordon Brown pledged to make the NHS more personal this week, promising quicker test results and better access to GPs, “because we know that being unwell is not just a nine to five problem.”

In his first speech to the Labour party conference as prime minister, Mr Brown promised an expansion of the screening services for breast and bowel cancer, quicker access to cancer treatment for more people, and £15bn (€21bn; $30bn) for research over the next 10 years. His long term plans include a regular health check for every adult in Britain.

“Our great achievement of the 1940s was a service universal to all. In 2007 we need a service that is accessible to all and personal to all,” said Mr Brown in an impassioned speech, during which he expressed his gratitude to the NHS for saving the sight in one of his eyes.

He added, “I want an NHS [that is] personal to you because you are seen by a consultant in a matter of days, not months; personal to you because there is a right to be given x ray results quickly and time to discuss your treatment; personal to you because we know that being unwell is not just a nine to five problem.

“And so we will make GP hours more friendly to families, open up opportunities to see a GP near your place of work as well as your home, expand walk-in centres [and] medical services at pharmacies, and ensure a better service from NHS Direct.”

The latest proposals mean that breast cancer screening will be available to all women between the ages of 47 and 73, an expansion from the current age range of 50 to 70. And from 2010 bowel screening will be extended from the present 60 to 69 age range to include men and women up to the age of 75.

The Department of Health has guaranteed that all patients with breast problems, not just those with suspected cancer, would get an appointment with a specialist within two weeks of being referred. Results from smear tests would be available within 14 days instead of the six weeks that more than half of women who are screened currently have to wait.

In addition, women who are referred for further investigation through the breast cancer screening programme—who are currently excluded from the 62 day referral to treatment guarantee given to women referred urgently by their GP—will be fast tracked and put on the same priority level, to ensure that they too get prompt treatment.

To tackle the problems of meticillin resistant Staphylococcus aureus and Clostridium difficile, Mr Brown promised extra funds for a “deep clean” of hospital wards. The number of matrons on wards will be doubled to 5000.

Alan Johnson, the health secretary, told BBC Radio 4’s Today programme ahead of his own speech to the conference that he intended to work with GPs and the BMA to develop a “much more convenient service” and that he did not want a “confrontational approach.”

He said, “The NHS was developed as a kind of monolithic organisation; it was a creature of its time, very centrally driven. That has changed. What we are trying to do . . . is to get local practitioners looking out towards their patients rather than up towards Whitehall for their tablet of stone.”

Commenting on Mr Johnson’s speech, Hamish Meldrum, the chairman of the BMA, said, “Mr Johnson’s words sound good, but we now have to see if they are followed by action.”

Annual check-ups aren’t needed, US study says

Janice Hopkins Tanne NEW YORK
Annual physical examinations, a staple of medical care in the United States for decades, cost too much and are not necessary for conveying messages on preventing illness, says a new study.

Patients get most messages on prevention through other visits, explains the study, published in the Archives of Internal Medicine (2007;167:1876-83). But gynaecological exams each year may be helpful for women, it says.

Ateev Mehrotra and colleagues from the University of Pittsburgh Medical Center examined data from 2002, 2003, and 2004 from the US national ambulatory medical care survey and the national hospital ambulatory medical care survey, which record visits made by patients with health insurance to office based physicians and to hospital outpatient departments for annual check-ups and gynaecological examinations.

During 2002-4 about 44 million US adults had an annual preventive physical check-up and about 19 million women had a preventive gynaecological examination each year.

Many tests are unnecessary and in total cost more than $350m a year, the authors say. A complete blood count, serum electrolytes test, urinalysis, and an electrocardiogram are often ordered as part of an annual check-up but are not necessary unless there is a reason to request them, Dr Mehrotra said. However, during gynaecological examinations women were likely to receive or be sent for evidence based tests such as mammography or cervical smear tests.

Although advice on prevention is sometimes given as a reason for annual check-ups, the researchers found that almost 80% of preventive messages were given when a patient visited for another problem during the same year.
Ten per cent of girls in England have HPV by age of 16

**Owen Dyer LONDON**

By the age of 16 at least 10% of girls in England have become infected with one or more strains of the human papillomavirus (HPV), a major study of HPV prevalence in girls and young women has shown.

Researchers from the Health Protection Agency tested 1483 women and girls aged 10 to 29 years from across England for four strains of the virus: types 6, 11, 16, and 18. Types 6 and 11 are associated with genital warts in particular, while types 16 and 18 are thought to be causative agents in an estimated 70% of cervical cancers. Their findings are reported in the *British Journal of Cancer* (doi: 10.1038/sj.bjc.6603955).

Doctors rank myocardial infarction as most “prestigious” disease and fibromyalgia as least

**Paul O’Grady**

*creator of Lily Savage* had a heart attack at 46

**Roger Dobson**

*ABERGAVENNY*

Fibromyalgia and anxiety neurosis are the illnesses with the lowest prestige among doctors, according to a survey of Norwegian doctors. The survey found that heart attacks top the prestige league, closely followed by leukaemia, and that neurosurgery is regarded as the most prestigious specialty (*Social Science & Medicine* doi: 10.1016/j.socscimed.2007.07.003).

“Results show that there exists a prestige rank order of diseases as well as of specialties in the medical community,” write the authors. “Our interpretation of the data is that diseases and specialties associated with technologically sophisticated, immediate and invasive procedures in vital organs located in the upper parts of the body are given high prestige scores, especially where the typical patient is young or middle-aged.” They say that any such ranking among doctors could have effects on practice.

In the study, the authors, from the University of Oslo and the University of Science and Technology, Oslo, sent questionnaires to 305 senior doctors, 500 general practitioners, and 490 final year medical students.

Respondents were asked to rank 38 diseases as well as 23 specialties on a scale of one to nine. The item concerning the prestige of diseases said, “Please give each disease a number based on the prestige you imagine it has among health personnel.”

The authors say that the prestige scores for diseases and for specialties were remarkably consistent across the three samples. Myocardial infarction, leukaemia, spleen rupture, brain tumour, and testicular cancer were given the highest scores by all three groups. Prestige scores for fibromyalgia, anxiety neurosis, hepatic cirrhosis, depressive neurosis, schizophrenia, and anorexia were at the other end of the range.

“The existence of a prestige rank order of medical specialties has been known for a long time,” write the authors. “Our results show that two different samples of physicians scored diseases according to prestige with only minor differences, and a sample of medical students in their final year scored them in much the same way. This is remarkable, as the prestige order of diseases is not openly debated, but must arise as a result of the numerous talks and actions going on in connection with the daily practice of medicine.”

“A widespread, and at the same time tacit, prestige ordering of diseases may influence many… decisions in the medical community, possibly without the awareness of the decision makers.”

---

**US vice president Dick Cheney has had four heart attacks**

---

**Zosia Kmietowicz**

*LONDON*

Reform of health and social services in England needs to slow down to allow the full engagement of staff and the public in the process, says a report from the independent health research organisation the Nuffield Trust.

The report, which examines the health and care needs of people in England in the next 15 years, says that reform of health and care services in England “is in danger of stalling.” But although further change is needed, this should proceed with a “re-engagement with consumers, health workers and citizens, in re-imagining and co-creating a shared vision of their future health and care services.”

Sandra Dawson, one of the report’s authors and professor of management studies at Judge Business School in Cambridge, said that morale among health and care staff was particularly low and they needed to feel involved in designing future services.

She welcomed the review of the NHS currently being conducted by the health minister Ana Darzi, which last week involved consultations with staff and the public. “It [the review] should be strongly supported, but we should not expect instant answers,” she added.

The Nuffield report echoes two other publications issued last week—by Derek Wanless and by the Institute for Public Policy Research—in calling for
with patients, says Nuffield Trust

the devolution of power from Whitehall and greater support for individuals, families, and communities to take control of their health and wellbeing by shaping local health policies.

The report says, “We can hope to replace a health and care system led from the centre with one based around a focus on patients and communities, connections—professional and organisational—rather than boundaries, and an emphasis on local rather than national solutions.”

It calls for policy makers to define a basic insurance package for health and social care, with information on which services are freely available and which can be bought through top-up insurance schemes or by paying for them.

Pam Garside, a management consultant who helped write the report, said that people know that certain services, such as infertility treatment and dentistry, have to be paid for to some extent. She took the view that other treatments able to be bought in this way needed to be clearly defined.

The report concludes: “While engagement at all levels may slow reforms, it is the only way to achieve lasting change. This does not mean that reform must move at the pace of the slowest; it demands bold vision and leadership, beyond the time-limits or political constraints of governments. Such visionary leadership must provide the motivation for the reformulation of professional values and public re-imagining of health, care and wellbeing in the 21st century.”

Engaging with Care: A Vision for the Health and Care Workforce of England is available at www.nuffieldtrust.org.uk.

Doctors get advice on rights of children and young people

Zosia Kmietowicz LONDON

Doctors in the United Kingdom have for the first time been given guidance on their roles and responsibilities when treating children and young people.

The General Medical Council, which regulates doctors in the UK, developed the standards after a three month consultation with children and adolescents aged under 18, doctors, parents, organisations, and the general public.

The GMC received more than 950 individual responses. Young people have also taken part in workshops around the UK and been involved in drafting the guidance.

Graeme Catto, president of the GMC, said, “This is the first time the GMC has set standards for doctors specifically about children and young people. Previously our advice has only referred to children and young people where their position is different from that of adults; this document recognises that children are individuals with rights that should be respected.”

He continued: “Young people told the GMC that doctors don’t always listen to them or take them seriously. We hope our new guidance will remind doctors of their ongoing duty to make an effort to communicate effectively with all their patients, including those who are under 18.

“The principles outlined in the guidance will provide a useful framework for doctors when they are faced with difficult situations—for example, respecting the rights of a young person to confidential treatment whilst being aware of the need to inform others if there is any indication of serious harm.”

The guidance says that the patient is the doctor’s primary concern but that doctors must also consider young patients’ parents and others close to them when they consult.

The booklet 0-18 Years: Guidance for All Doctors has been sent to all doctors in the UK and is available at www.gmc-uk.org.

DOCTORS’ RESPONSIBILITY TO CHILD PATIENTS: CASE HISTORY

Your patient is a 2 year old boy whose parents are divorced. He lives with his mother, who says she doesn’t want the father to know about her medical care or that of her son. If the father asks to see his son’s medical records, what should you do?

You should let those with parental responsibility have reasonable access to their children’s records if the child or young person lacks capacity or he or she consents, and such access is not against their interests. Divorce does not affect parental responsibility, and you should usually allow both parents reasonable access.

Advice on avoiding peanuts in pregnancy should be withdrawn

Zosia Kmietowicz LONDON

Department of Health advice to pregnant women with a family history of atopic diseases to avoid eating peanuts and food that contains peanuts and not to give such food to their children until the age of 3 years is out of date and should be immediately withdrawn, says a report from the House of Lords.

The health department advice, which was first issued in 1998 and is repeated in government booklets given to pregnant women and new parents, is totally without evidence, the House of Lords Science and Technology Select Committee heard during its inquiry into allergy in the United Kingdom.

Avoiding food that contains peanuts in early life could in fact be helping to fuel the rise in peanut allergy seen in the UK, says the report. The prevalence of peanut allergy in England increased by 117% between 2001 and 2005, and an estimated 25,700 people are affected. But similar increases in prevalence have not been found in developing countries.

Gideon Lack, head of paediatric allergy at Evelina Children’s Hospital in London, told the committee that a number of recent epidemiological studies had indicated that early peanut consumption in countries such as Israel was associated with a low incidence of peanut allergy in the population. These observations had led many academics to say that exposing a child’s immune system to peanut allergen at an early age might result in tolerance.

Baroness Finlay of Llandaff, chairwoman of the committee, said, “We have serious doubts about the advice given to some pregnant women to avoid eating peanuts. A growing body of evidence suggests that in countries where peanuts form a major part of the diet of pregnant women and young children there is actually a lower incidence of peanut allergy in later life. The government should withdraw this advice with immediate effect.”

The select committee’s report, Allergy, can be seen at www.parliament.uk.
Media claim allocation of organs to Saudi patients was unfair

Annette Tuffs HEIDELBERG

The University Hospital of Kiel, in northern Germany, has been criticised for transplanting livers from cadavers to two Saudi patients, ahead of other, native German patients who had been on the waiting list longer.

The Saudi patients had been meant to receive a transplant from relatives, but they benefited from a recent change in the rules of Eurotransplant, the body that co-ordinates transplant allocation across seven European countries, propelling them to the top of the waiting list, even though they had only recently arrived in Germany and had a donor relative lined up.

Under the rule change, patients are given scores as to the urgency of their case that are based solely on laboratory blood test results (creatinine and bilirubin concentrations and prothrombin time). The score is given higher priority than the length of time the patient has been waiting for a transplant. The system, known as the model for end stage liver disease (MELD), is used in the United States by the United Network for Organ Sharing.

Eurotransplant, which coordinates transplantations in Germany, Austria, Belgium, Netherlands, Luxembourg, Slovenia, and Croatia, also does not distinguish between patients who are long term residents of its member countries and patients who have recently arrived. It has a rule that no more than 5% of organs should go to non-residents but has no means to enforce it.

Criticism of the Kiel hospital began in August, when the television programme Monitor reported that the Saudi patients had been given preference over German patients in return for substantial payments.

The hospital confirmed that two Saudi patients had received cadaver organs in 2007, although they were originally supposed to receive transplants from living relatives who had accompanied them to the hospital.

Bernd Kremer, the hospital’s medical director, said, “According to German law we have to put all patients, including ones expecting organs from a living donor, on a waiting list for a cadaver organ, regardless of whether they are German or come from abroad.”

UK hip fracture audit is launched to improve care and to cut costs

Susan Mayor LONDON

A new UK-wide audit has been launched to improve the care of patients with hip fracture. The audit aims to help reduce the currently low and variable rates of investigation and treatment of osteoporosis in elderly people who are admitted to hospital with fragility fractures.

The audit system, known as the national hip fracture database, will gather data submitted voluntarily by hospitals around the United Kingdom. Its design is based on an audit of myocardial infarction care, the myocardial infarction national audit project (MINAP), which has had a major role in improving the management of heart attack.

The hip fracture database will audit hospitals against six standards proposed in a guide to best practice, The Blue Book on the Care of Patients with Fragility Fractures, published last week by the British Orthopaedic Association and the British Geriatrics Society. The standards include admitting all patients with hip fracture to an acute orthopaedic ward within four hours of presentation and performing surgery within 48 hours of admission on all patients who are medically fit.

To prevent hip fractures, one of the audit standards is the assessment of all patients presenting with fragility fracture to determine their need for antiresorptive treatment to prevent future osteoporotic fractures.

The report warns that 75 000 hip fractures occur each year in the UK, costing the NHS

UK considers moving to new system to increase organ donation

Clare Dyer BMJ

The UK government is considering moving to a system where people will be presumed to have consented to the use of their organs for transplantation unless they have opted out.

The health secretary, Alan Johnson, has asked the organ donation task force to look at the ramifications of moving from the present “opt-in” system, in which organs can be used only if people have given their prior consent, to the sort of opt-out regime currently operating in some other countries, including Sweden and Austria.

The task force, set up in 2006 to look at barriers to organ donation, will examine the legal, ethical, practical, and medical issues, including whether the family of somebody who has died should be given the final say on organ donation. At present the family’s consent is required unless the potential donor has signed up to the organ donor register or otherwise expressed a wish to donate organs.

Mr Johnson said, “We know that around 8000 people in the United Kingdom need an organ transplant, but only 3000 transplantations are carried out each year. With more than 400 people dying every year waiting for a new kidney, heart, lung, or liver, we need to do everything possible to increase organ donation.”
Enter the circle, invites Seamus Heaney

Lynn Eaton LONDON
The Scottish sculptor David Annand stands with his statue the Listening Lady, which sits in a circular frame and acts as a resting place for patients and visitors at the Marie Curie Cancer Care Hospice in Belfast.
The seat is inscribed with the lines:
Still yourself, take time, be at rest.
Enter the circle, unalone, a guest.

Better access to drugs could save 10 million lives a year, says UN expert

John Zarocostas GENEVA
Better access to drugs, especially in poor countries, could save 10 million lives each year, four million of them in Africa and South East Asia, an independent UN expert said as he unveiled a set of draft guidelines for pharmaceutical companies on access to drugs.
The 50 draft provisions drew a mixed response from interested parties. They were welcomed by groups that advocate for access to affordable drugs but were strongly criticised by the industry.
Announcing the guidelines, Paul Hunt, the United Nations’ special rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health, said, “Almost two billion people lack access to essential medicines. Improving access to existing medicines could save 10 million lives each year.
Professor Hunt, who is professor at the department of law and the human rights centre at Essex University, continued: “Access to medicines is characterised by profound global inequity, as 15% of the world’s population consumes over 90% of the world’s pharmaceuticals.” The 12 pages of recommendations, which are available for public comment until the end of 2007, are likely to be finalised next year, he said. They were drafted “to help pharmaceutical companies enhance their contribution to these vital human rights issues” and “to assist those who wish to monitor the human rights performance of the pharmaceutical sector in relation to access to medicines.”

The draft guidelines are at:
www2.essex.ac.uk/human_rights_centre/ith

Increase organ donation

“I want to see organ donation and transplant rates start to rise and match the rates seen in some other European countries, enabling us to save many more lives. This is a sensitive issue, but it is vital that all possible options for increasing the number of organs available for transplant are explored.”
A recent survey by Ipsos MORI for the Human Tissue Authority found that although 68% of respondents said they were likely or certain to donate their body, organs, or tissue, only 5% had taken the necessary steps to do so (BMJ 2007;335:533, 15 Sep).
The organ donation task force has a remit covering the whole of the UK. Last year, when legislation on organ donation was going through the Scottish parliament, members rejected a move to require people to opt out of becoming donors.
Vivienne Nathanson, the BMA’s head of ethics and science, said the association favoured a system of presumed consent, but with safeguards.
“Before any changes go ahead, however, it is essential that a public information campaign is launched so that people are completely aware of the choices they can make.”
The Liberal Democrats’ science spokesman, Evan Harris, said he would re-table an amendment introducing an opt-out scheme when the Human Tissue and Embryo Bill comes before parliament next year.
Doctors should speak out on climate change, expert says

Bob Roehr CHICAGO

Doctors and health workers have a duty to draw attention to climate change and try to change people’s behaviour to avert disaster, an expert on the issue told a conference in Chicago last week.

Anthony McMichael, director of the National Centre of Epidemiology and Population Health at the Australian National University, Canberra, said that doctors had a particular responsibility because they had influence and because the health sector would have to deal with some of the worst effects of climate change.

Addressing the annual interscience conference on antimicrobial agents and chemotherapy in Chicago, Dr McMichael acknowledged that 5-10 years ago the topic would not have been on the agenda, “but the evidence is accruing rather more rapidly than we would have anticipated.”

Speaking to the BMJ he said that the medical profession was still held in high regard and had influence. He pointed to its leadership on the nuclear disarmament debate decades ago as an example of what could be done with that influence. “Planet [climate] change and its consequences to human health now loom probably orders of magnitude larger than the nuclear debate.”

The health sector needs to understand that it will have to bear many of the repercussions of global climate change. “We’ve got work to do to try to head off aggressive risks before adverse health occurs,” he said.

He added, “We’ve got to get more imaginative about working with other sectors, other arms of government, making the argument that every ministry is a health ministry.

“The health sector has been much too separatist in the past. It has been thinking that all it has got to do is run a healthcare system and traditional public health. Climate change is telling us that no, that’s not good enough. We’re going to have to be more imaginative, more collaborative, and be prepared to look to a more distant future as well as deal with the problems that press on us in the here and now.”

Giving the keynote speech to the conference, he reviewed projected patterns of how temperature and rainfall are likely to change throughout the world and how such change might directly affect the prevalence of human infectious diseases. There are likely to be indirect effects as well, he said, with shifting patterns of diseases that affect plants and livestock.

One example he cited was the fluctuation of what is called the El Niño or La Niña effect of warmer or cooler ocean currents, which in turn affects rainfall in Pacific rim countries. Rainfall has a major effect on the mosquito population and the incidence of dengue fever. Another example of the effect of climate on the incidence of diseases was apparent in China. “Over the last few decades the critical freezing zone that sets the limit on snails that are the intermediate hosts of schistosomiasis has been shifting northwards, and there has been a report of increased incidence of disease.” The change could put an additional 21 million people at risk.

Most examples of the effects of climate change on health came from the developing world, Dr McMichael said.

IN BRIEF

US Congress reauthorises FDA for five years: President Bush is expected to sign a bill that raises by 25% the fees paid by drug companies for the Food and Drug Administration to review new drugs. It also sets up a computerised surveillance system for adverse events that uses data from pharmacies and insurance companies. The bill gives the FDA the power to make companies conduct trials of drugs that are already approved. (See BMJ 2007;335:471.)

HIV vaccine trial is ended: Merck has halted trials of its HIV vaccine, generally considered one of the most promising candidates. Company officials said that the adenovirus vaccine had conspicuously failed to prevent infection in a study of 3000 high risk volunteers in North and South America, the Caribbean, and Australia.

Racial disparity in infant mortality widens in the US: Disparity in mortality between black and white infants in the United States has widened (American Journal of Obstetrics and Gynecology doi: 10.1016/j.ajog.2007.06.006). The study, which looked at data from 1985-8 and 1995-2000, showed that white infants born before term had greater gains in survival over time than black infants. Each year in the US about 3300 more black infants die than would be expected.

Campaigning doctors suffer arrest and death: Doctors were among trade unionists who were killed, beaten, arrested, or dismissed last year for their involvement in activity to defend labour rights, says a global survey by the International Trade Union Confederation. This included the murder in Iraq of a health union campaigner and the injury by police of 22 striking doctors in Nicaragua. (See www.ituc-csi.org.)

Czech doctors strike over pay: GPs in the Czech Republic staged their third strike action this year over low pay, by closing surgeries for one day last week. GPs receive 36 koruny (£0.91; €1.30; $1.80) monthly for each registered patient, and just 4.5% of the total healthcare budget is allocated to GPs.

Tackle health inequality as first step to “personal NHS”: Any attempts to create a personalised health service should start by identifying the millions of people who are not accessing the services they need, says a report from the NHS Confederation, In Sickness and in Health (see www.nhsconfed.org).

Larger parts of China are now warm enough for the snail that spreads the schistosomiasis parasite
Hillary Clinton unveils plan for healthcare reform at a cost of $111bn

Fred Charatan FLORIDA

Hillary Clinton, nominee for the Democratic party’s presidential candidate and New York senator, last week announced her plan to reform health care. She would require insurers to provide coverage for anyone who applied and would bar companies from charging people who have greater healthcare costs more for their premiums.

Speaking to the annual convention of the American Association of Retired Persons, in Boston, she said, “Health care should not be a privilege for a few, but a right for every single person. There are 47 million uninsured in this country, and covering them is a moral imperative.”

Mrs Clinton told a story about a constituent who came to her after her son was diagnosed as having leukaemia. The insurance company had agreed to pay for a stem cell transplant but refused to pay for the search to find a suitable donor. But after Mrs Clinton took up the cause the insurer complied.

“It should not take a US senator for a parent to get the health care [that] their son or daughter needs,” she said.

If elected, she vowed to accomplish her goal in her first term. The estimated cost would be $111bn (£55bn; €80bn). She has replaced the complexities of her last effort 14 years ago in favour of simplicity, cost control, and individual consumer choice.

Healthcare giant advertises to children in Australia’s classrooms

Ray Moynihan BYRON BAY, AUSTRALIA

The multinational drug and medical device manufacturer Johnson & Johnson has been advertising its products in a resource book used by children in Australian classrooms.

The book, BodyWhys, is sponsored by Johnson & Johnson and contains several advertisements for Johnson & Johnson products, including tampons, sanitary pads, toothbrushes, and pimple cream.

Along with the advertisements, BodyWhys, which was recently distributed to 10 year old children in a state school in Sydney’s wealthy eastern suburbs, contains text about personal development.

Johnson & Johnson says it has been sending copies of the book to schools on request for several years. This year more than 130 private and public schools across Australia have received copies.

In a section about skin care the book suggests that “you should try a preparation for your face that has been specially formulated for teenage skin, for example, Clean & Clear,” a Johnson & Johnson product. Similarly, the sections on teeth and gums include advertisements for Johnson & Johnson toothbrushes and dental floss.

A spokesperson for Johnson & Johnson Pacific said the BodyWhys book was made available to schools “to address the need for education and product information.”

Miranda Burne provided research assistance.
Nightly dialysis looks a promising alternative for haemodialysis patients

Frequent haemodialysis at night may be better than traditional three times a week treatments, according to a preliminary trial from Canada. The 52 participants were all patients on long term dialysis, mostly in self care or home dialysis programmes. Patients who switched to six overnight sessions a week had a significantly lower left ventricular mass than controls after six months (difference 15.3 g, 95% CI 1.0 to 29.6). They also had lower systolic blood pressure (adjusted mean difference 14 mm Hg, 3 to 26), and they were more likely to have reduced or stopped their anti-hypertensive drugs. The new regimen had no effect on overall quality of life, but the authors found a clinically relevant improvement in quality of life related to kidney disease.

The trial was too small to look at the effect of nightly haemodialysis on mortality or cardiovascular events. But left ventricular mass is a reasonable surrogate for the moment, say the authors. Bigger trials are on the way, although none aims to recruit anything like the 5000 patients who did both forms of exercise achieved an extra reduction of 0.46 percentage points, P=0.038. Participants for six months. Aerobic exercise reduced haemoglobin. But these activities are even more effective when combined, according to a randomised trial.

Participants exercised three times a week for six months. Aerobic exercise reduced their glycated haemoglobin concentrations by 0.51 percentage points compared with inactive controls. Resistance training with weights had a similar effect (change −0.38 percentage points, P=0.038). Participants who did both forms of exercise achieved an extra reduction of 0.46 percentage points compared with the aerobic group and 0.59 percentage points compared with the weight training group. This extra glycaemic control could be clinically important say the authors.

Global child mortality is falling too slowly

Estimating child mortality has always been an inexact science because data from so many countries are old, patchy, and unreliable. In an attempt to get a clearer picture, researchers did a thorough analysis of all available data from 172 countries, including new sources as well as data collected routinely by the World Health Organization and Unicef.

They found that deaths in children under 5 decreased from 13.5 million (95% uncertainty interval 13.4 to 13.6) in 1980 to an estimated 9.7 million (9.5 to 10.0) in 2005, a slow decline that will miss millennium development targets set for 2015. If trends continue as they are, child mortality will have fallen by only 27% between 1990 and 2015, far short of the 67% set in millennium development goal 4. Despite major international efforts, we don’t seem any better at saving children than we were 20 years ago, say the researchers. The trends are particularly disappointing in west, east, and central Africa, where the absolute number of deaths each year has risen by more than a quarter since 1970. By 2015, more than half of all child deaths worldwide will occur in sub-Saharan Africa. This figure was only 19% in 1970.

_Lancet_ 2007;370:1040-54

_Mortality in Children under 5 years in 2005_

Each percentage point reduction means 15-20% fewer cardiovascular events.

The 251 participants in this trial were quite heavy, with an average body mass index of around 35. About a quarter of patients who exercised had musculoskeletal aches and pains or injuries. The exercise had no effect on their serum lipids or blood pressure.

Even so, this trial makes it clear that exercise is an important part of the treatment for type 2 diabetes, says an editorial (p 423). Doctors should remember to prescribe it.

Ann Intern Med 2007;147:357-69

Exercise is an important treatment for type 2 diabetes

We know that regular exercise can help people with type 2 diabetes achieve better glycaemic control. Aerobic activities such as cycling or resistance training with weights can bring down serum concentrations of glycated haemoglobin. But these activities are even more effective when combined, according to a randomised trial.

Women taking teratogenic drugs need contraceptive advice

Women taking potentially teratogenic drugs may be missing out on contraceptive counseling, say researchers from the US. In an analysis including nearly half a million women of childbearing age, one in six were prescribed a potentially teratogenic drug in 2001. For almost half of these women, the researchers could find no documentary evidence of counseling, prescriptions for contraceptives, or sterilisation despite a thorough search through healthcare databases recording prescriptions, outpatient visits, and hospital admissions. One percent of women prescribed a teratogenic drug were pregnant within three months. Women who used reliable contraception were the least likely to get pregnant. Antibiotics, benzodiazepines, and psychiatric drugs were the most common potentially harmful drugs prescribed to the women in this study.
These authors say their data sources were limited and they could have underestimated the extent of contraceptive advice available. They would certainly have missed any women using condoms, which don’t need a prescription. But it is still likely that many women are inadequately informed about the risks of an unintended pregnancy during treatment with many commonly used drugs. *Ann Intern Med* 2007;147:370-6

**US doctors must become the voice of the poor**

The US has a dismal record on health, despite outspending by a considerable margin every other developed nation in the world. Americans at the lower end of the socio-economic spectrum crystallise around single problems such as breast cancer and autism, while the poor die young from complications associated with smoking and substance abuse.

This must change, he writes. Large gains for the whole population will come only after a concerted effort to deal with the needs of Americans at the lower end of the socioeconomic spectrum. Health professionals should go back to basics and become champions of the public health. To do nothing is to accept the US position at the bottom of the league tables on health, when in so many other areas only first place will do. *N Engl J Med* 2007;357:1221-8

**Triglycerides have an independent effect on risk of heart disease**

The evidence is mounting that the serum concentration of triglycerides is an independent risk factor for coronary heart disease. The latest data are from nearly 14,000 young Israeli men who took part in a prospective cohort study with a mean follow-up of more than 10 years. The authors measured triglyceride concentrations twice, so they were able to track the effect of changes on the risk of heart disease.

Men with high values at the start of the study were significantly more likely to develop heart disease—detected by angiography—than men with lower values. But their risk fell if the second triglyceride concentration five years later was lower than the first. An increase in triglyceride concentrations between the two tests was associated with increasing risk. All findings were adjusted for known risk factors including other serum lipids. Men with consistently low concentrations of triglyceride had the lowest risk of heart disease.

An editorial says these results are important, not least because triglycerides are so closely linked to obesity (p 425). Losing weight and taking more exercise is one of the best ways to keep triglycerides under control. In this study, lower concentrations were also associated with eating a decent breakfast. *Ann Intern Med* 2007;147:377-85

**Mosquito nets reduce child deaths in Kenya**

A new study has confirmed that bed nets treated with insecticide are lifesaving for children living in sub-Saharan Africa. It showed that a Kenyan national programme to increase coverage between 2004 and 2006 was accompanied by a 44% reduction in deaths in young children who slept under a net, compared with those who didn’t (adjusted rate ratio 0.56, 95% CI 0.33 to 0.96).

The analysis was confined to children aged under 5, the group most likely to die from malaria. In 2004, only 7% of these children had a bed net. The proportion increased to 67% by 2006 thanks to a combination of strategies, including subsidising the sale of nets on the high street, offering more heavily subsidised nets to pregnant women at clinics, and giving nets away free to all young children. The authors estimate that on average every 1000 bed nets save seven lives. The benefits are likely to be greatest for children living in areas where transmission of malaria is high.

Bed nets treated with insecticide are clearly an effective way to protect children from potentially lethal malarial mosquitoes, says the authors, and donors who pay for them should consider their money well spent. *Lancet* 2007;370:1035-9

**Worries remain over safety of repeated antenatal steroids**

Corticosteroids are an established treatment for women at risk of premature labour and delivery. Current guidelines recommend a single dose, because of doubts about the potentially harmful effects of repeated doses on newborns and their later development.

Long term reports from two randomised trials are generally reassuring. Children aged between 2 and 3 years who had been exposed to multiple doses of antenatal steroids had similar developmental and growth outcomes to controls exposed to just one. But authors of this Australasian trial noted a slight increase in attention problems associated with repeated doses of steroids. It could be a chance finding, but further follow-up is planned. Eight other aspects of the children’s behaviour were unaffected including emotional reactivity, sleep, and aggression.

The only other notable finding was a nonsignificant increase in the risk of cerebral palsy in children exposed to multiple doses of antenatal steroids in the American trial (6/206 (2.9%) vs 1/195 (0.5%), relative risk 5.7, 95% CI 0.7 to 46.7).

Both trials have already reported that babies given repeated doses have healthier lungs at birth, and many units already allow repeated dosing. They should proceed with caution pending more information about the possible link with cerebral palsy, says an editorial (p 1248). *N Engl J Med* 2007;357:1179-89, 1190-8
MATERNITY SERVICES

HOW FAR IS TOO FAR?

Any change to local hospital services raises concerns about safety and accessibility, but plans to close the obstetric department at an Oxfordshire hospital have stirred up particularly strong feelings, as Adrian O’Dowd reports.

Many acute trusts in England are currently considering reconfiguring some of their services. All over the country, battle lines are being drawn as patients and doctors fight to save local hospitals, and in one case the dispute has become so intense that the health secretary has been called in to make a judgment.

One of several changes proposed by Oxford Radcliffe Hospitals NHS Trust is to close its consultant led obstetrics department at the Horton General Hospital in Banbury and replace it with a midwife led birthing unit, which would be the country’s largest such unit. The trust argues that change has come because of long held concerns over the long term safety and sustainability of medical staffing of children’s services at the Horton. It claims the changes overall will cost the trust an extra £593,000 (€893,000; $1.2m) annually, alongside a capital programme of £7m investment at the hospital, but those opposed to the changes have questioned the figures and believe cost cutting is playing a part in the trust’s motives.

These plans have led to strong opposition, as shown by a four month consultation held last year, a petition opposing the changes signed by more than 15,000 people, and a statement condemning the move signed by 86 general practitioners.

In response to concerns, the trust set up two clinical groups (including general practitioners, consultants, and midwives) to consider the proposals in more depth. A stakeholder group including representatives of patient, community, and public bodies, however, rejected the clinical groups’ support for the trust’s proposals, saying they “represented a significant downgrading of access to services and a worsening of choice for women and children.”

The Oxfordshire joint health overview and scrutiny committee then considered the arguments, concluded the changes were not in the best interests of local people, and referred the issue to the health secretary.

Local concerns

The argument centres around the safety and efficiency of a midwife led unit compared with an obstetrics led unit because, should the change go ahead, the new unit will be 26 miles from the nearest consultant unit at the John Radcliffe Hospital.

The issue of distance was highlighted recently by a study in the *Emergency Medicine Journal* which found that the further seriously ill patients had to travel to receive emergency
there will not be any accurate figures for outcomes in such units until 2009, when the National Perinatal Epidemiology Unit study is due to report.

Feelings are running high over this issue, he adds, saying: “This is not a matter of local sentiment and convenience, but an issue of fundamental safety common to all localities at an hour’s remove from a major hospital.”

Melanie Every, Royal College of Midwives’ regional manager for the south, rejects the accusation that midwife led units are not proved to be safe.

“There is no hard evidence that they are unsafe either,” she says. “There is a lot of evidence that women’s labours progress better with one to one care from a midwife that they know. You are much more likely to get that in a midwife led unit.

“For Horton, the proposals need to ensure that women have real choice so that those women who want to have a consultant led service can have that and that you’ve got the appropriate back-up services if you do need to transfer women from a midwife led unit to a consultant unit.”

The Horton is not an isolated situation, she says, adding: “A number of areas of the country are looking at concentrating their consultants’ services on one site for all sorts of reasons, but mainly to do with a shortage of paediatricians and making sure they have a high quality service on one site for those neonatal babies that really need it. Therefore, the other sites are likely to be midwife led.”

Horton symbolises many other ongoing debates in the country, says Jim Thornton, professor of obstetrics and gynaecology at the City Hospital in Nottingham. Professor Thornton is about to publish the findings of a study of the national situation on reconfigurations for the campaigning pressure group Doctors for Reform.

“The Horton closure is typical,” he says. “Despite the fact that England already has much larger maternity units than other west European countries, we have discovered plans, at various stages of development, for consultant maternity unit mergers in nearly all strategic health authorities. They affect units of all sizes.

“If they are all followed through, England will have a few consultant units delivering fewer than 3000 women per year and many delivering two or three times that amount.”

Peter Fisher, a retired consultant in general medicine at the Horton hospital, who is now president of the NHS Consultants Association, is also worried about the safety of the changes being proposed at the Horton.

“The major risk (and psychological trauma) would be in those cases needing emergency transfer in labour from a Banbury midwife led unit to Oxford,” says Dr Fisher. “We now have a situation where the trust claims that its proposals would carry less risk than the current services might in two years’ time. Whereas virtually everyone else takes the view that the proposals carry unacceptable risk.”

The Oxford Radcliffe trust is adamant that it is doing the right thing and expects that a full review will be instigated now that the health secretary has referred the issue to the Independent Reconfiguration Panel, which provides advice on changes in NHS service. The panel will report back early in the new year, and if it supports the trust board’s decision to approve the proposals the changes will be phased in over 12-18 months.

A trust spokesperson said: “It’s not been driven by a desire to drive down costs. It was driven by concerns about clinical safety. All we are doing is moving the obstetricians to another of our hospitals. The obstetrics service remains, it simply moves from one site to another.”

The issue is far from settled. Adrian O’Dowd is a freelance journalist adrianodowd@hotmail.com Competing interests: None declared.
The view that birth outside hospital is less safe than hospital birth prevails despite evidence to the contrary. Discussion about maternity services often becomes polarised around the comparative safety of different places of birth, and argument over a single measure of safety, perinatal mortality. The dominance of the medical view of birth has led to an exponential rise in medical and surgical interventions in childbirth in most of the developed world and parts of the developing world. The risk of unnecessary intervention, for mother, baby, and future generations is ignored.

One consequence is the steady and continuing rise in the rate of caesarean sections. In the developed world (including Europe, North America, Japan, Australia, and New Zealand) the proportion of caesarean births is 21.1% (range 6.2% to 36%). Yet, as Bertran and colleagues concluded: “higher caesarean section rates do not confer additional health gain.” Caesarean section is associated with a higher maternal mortality, and complications in future deliveries.

Reducing interventions

Midwifery led care, particularly out of hospital care, may reduce the risk of intervention and increase the possibility of normal birth. A systematic review of the outcomes of home birth indicates that planned home birth is no less safe than hospital birth for women and babies without complications and that planned home birth is associated with a lower intervention rate and provides a more positive experience for many women.

The development of birth centres has provided a further choice for women about place of birth. Birth centres have also provided clinical environments where midwives can fully use their skills and provide support for normal birth avoiding unnecessary intervention. One structured review of studies of women and their babies who planned to give birth in a birth centre in developed countries found no reliable evidence about clear benefit or harm associated with birth centre care. Another review based on Cochrane guidelines found lower intervention rates for women in midwifery led out of hospital birth centres, although there were concerns about the quality of the individual studies.

Uncontrolled social experiment

The move to have all women give birth in hospital was one of the biggest uncontrolled medical and social experiments of the 20th century. From 1954 to the 1980s in the UK the percentage of births at home fell from about 35% to 1%. In most of the developed world close to 100% of women give birth in hospital. The shift has resulted in a loss of social support, which can not be supplanted by professional care in the hospital.

Much of the motivation for the drive to hospital birth was the belief that this would increase safety and reduce the inequalities of care. The move to hospital birth was never evaluated and an increase in safety or a reduction in inequalities in outcomes has never been proved. Significant differences in both perinatal and maternal mortality remain between different groups of women and different populations.

Government policy in England in the early 1990s recognised a growing sense of discontent with the maternity services. This discontent should not have been surprising. The institutionalisation of birth was associated with several problems, particularly where hospitals are large. There is a tendency to dehumanisation and difficulty in providing personal care appropriate to individual needs. Midwifery had been taken from its community base to the fragmented care of hospital and lost professional autonomy and influence.

Although there is some overlap in their sphere of practice, midwives and doctors bring different philosophical, approaches, skills, and expertise to maternity services. Midwifery is based on the need to respect, recognise, and support physiological processes while recognising deviations from the norm. An important aspect of effective midwifery is supporting a positive transition to parenthood and family formation. Midwifery care is more likely to provide a positive experience of care and to reduce the intervention rate when continuity of carer is provided. Obstetrics is concerned with the care of mothers and their babies when complications occur or are likely. Women and their babies need midwifery care and some additionally need obstetrical care. The system needs both approaches in balance.

Since the 1980s new policy in many parts of the world has started to improve maternity care and bring the system back into balance. This includes provision of home birth, the development of midwife led services, birth centres both inside and outside of hospital, and the development of continuity of care to women and their families.

A one size fits all approach to maternity care is neither advisable nor sustainable. Women at low risk should be offered home birth, as this may confer considerable benefits for them and their families. Some women may wish to give birth in hospital with midwifery led care. A network of services is required so that women may be referred and transferred when necessary and cared for by the appropriate professional. Consultant obstetricians have valuable skills that need to be concentrated on the care of women with complicated pregnancies. Safer maternity services are those that recognise and respond to the effects of inequalities and ethnicity, recognise the risk of unnecessary interventions, and support all professionals to play their full part in care.

Competing interests: None declared.
The UK government claims it is trying to give women more choice by converting local maternity units to midwife led services. Lesley Page believes such units improve the birth experience, but Jim Drife remains worried about the risks of delivering outside hospital.

Maternal complications during childbirth are no less frequent than they were in the past. National audits in Scotland report life threatening emergencies once in 200 births. The most common, severe haemorrhage, occurs once in 300 births and is usually unpredictable. Of 156 such cases in 2004, only a minority were antepartum haemorrhage, but 32 women bled during labour and 116 after delivery. Prompt treatment saves lives every day across the UK, and national maternal mortality is low because emergencies are managed effectively.

Nevertheless, pregnancies are now classed as high or low risk (a false dichotomy as most are in between). Risk classification is based on the history given by the woman at booking. This is no easy task. A woman in her first pregnancy does not have an obstetric history. Family history is often incomplete. Complications such as pre-eclampsia and fetal growth restriction cannot be predicted. The result is that women labelled low risk have a higher corrected singleton perinatal mortality than high risk women.6

Research on performance
Evidence on safety of midwife led units is lacking. A 2005 Cochrane review found no trials of freestanding birth centres.7 There was, however, a trend towards higher perinatal mortality in “home-like settings” with a relative risk of 1.83 (95% confidence interval 0.99 to 3.38). An earlier systematic review comparing continuity of midwifery care with standard maternity services found that midwifery care was associated with an increase in perinatal death “bordering on statistical significance” (odds ratio 1.60; 95% confidence interval 0.99 to 2.59).8 In both reviews the confidence intervals included 1.00 (though only just), so the trends were not significant. Nevertheless, they should worry those who want to change patterns of care.

Many UK maternity hospitals have a consultant unit and a midwife led unit in the same building, and staff prefer this arrangement. Even in such units, however, the evidence is not entirely reassuring. In the midwife led unit of the Stockholm Birth Centre (one floor below a standard delivery ward) perinatal mortality among primiparous women was significantly higher than among Swedish women receiving standard care (relative risk 1.8; 1.06 to 3.00). For multiparous women, rates were not significantly different.9 When data for first pregnancies were recalculated, the rate of fetal death in labour in the birth centre was 1 in 493, over seven times higher than the rate of 1 in 3779 with standard care in Sweden.10

Free standing midwife led units may be some distance from medical help. Transfers may save lives but are often precautionary and have a negative psychological effect on women.11 Rates of transfer before labour in the Cochrane review were 29-67%.12 In Stockholm the transfer rate during labour was 18%.13 In a Scottish unit rates were 30% before labour and 27% during labour for primiparous women, and 22% and 10% for multiparous women.12 In a US study of midwife led units in the 1980s, 7.9% of women had serious complications in labour and transfer rates among primiparous and multiparous women were 29% and 7% respectively.13

The National Perinatal Epidemiology Unit says: “a structured review carried out in 2005 concluded that high quality evidence was needed about whether there are important differences in experiences and outcomes for women and babies in these alternative locations and systems.”14 Others have also called for better evidence: “if women at low obstetric risk are offered a choice between free-standing MLMU (midwife led maternity units) and hospital, they should be aware that the safety and effectiveness of delivery in the two settings has not been reliably compared.”15

It is disturbing that in an era of evidence based medicine, midwife led units are being promoted before their safety has been established. The attractions of a relaxed environment and non-intervention are easy to understand, but most women put the highest premium on safety for their baby. Last year the National Perinatal Epidemiology Unit began an evaluation of alternative locations for labour and birth.16 Further change should await reliable evidence on safety.

COMPETING INTERESTS: JD is an obstetrician in a tertiary centre and works on the labour wards. He is an obstetric assessor for the national Confidential Enquiry into Maternal Deaths. All references are on bmj.com

WHERE DO YOU STAND ON THE ISSUE?
Vote now on bmj.com
MEDICINE AND THE MEDIA

Who are the doctor bloggers and what do they want?

Medical blogs are sometimes seen as just rants about the state of health care, but they have also been credited with spreading public understanding of science and rooting out modern day quacks. Rebecca Coombes checks out the medical blogosphere.

In “internet time” blogging has been around for almost an eternity. Now, with the possible exception of the odd intransigent high court judge, blogging has achieved household name status since catching the public’s imagination nearly a decade ago.

The medical “blogosphere” is an especially crowded firmament. The opportunity to access raw, unfiltered material, to post instant comments, and to share information with a (often niche) community has become an addictive pastime for many doctors. The field has developed to the extent that devotees rely on their favourite blogs as their first port of call for topical opinion and debate. Taken as a group, the medical bloggers—the popular ones, at least—are overwhelmingly younger men, and many have a typically masculine geeky humour.

But the field is far from just a playground for the young. For example, David Colquhoun, professor of pharmacology at University College London, is 71 and now a celebrated blogger in his field. Professor Colquhoun thinks that a blog’s power lies in its independence. Unlike newspapers, blogs don’t feel bound to present a balanced picture, he says, “which, only too often, means giving equal space to people who believe the earth is flat and those that don’t.”

“On a blog I can just give my view. It’s obviously that—and people can take it or leave it. Also, bloggers often seem to be better at investigative journalism than journalists are. All sorts of facts about dodgy practices appear on blogs long before they reach the regular magazines or papers; that is both fun and useful, I think.”

Today annual awards are given for the best medical blogs—including a prize for the best literary medical blog—and competing websites offer rankings of the best blogs. The site www.edrugsearch.com ranks more than 400 of the most popular blogs on health and medicine. It’s hard to gauge just how popular some of these sites are, as top rated bloggers—such as BMJ columnist Ben Goldacre, who writes www.badschience.net—keep this a closely guarded secret. Many of the most quoted and linked-to blogs are by anonymous doctors, who shelter under fake names to vent opinions on anything from political interference in the NHS to how science is misrepresented in the media.

NHS Blog Doctor (http://nhsblogdoc.blogspot.com), by a general practitioner writing under the pseudonym of Dr John Crippen, is described as an “extremely depressing” look at the NHS. Dr Rant (www.drrant.net) does what it says on the tin: rant about medicine related topical issues, laced with lots of strong language. These sites examine political interference, root out modern day quacks, correct ignorant journalism, digest interesting stories, or comment on big official reports, for example. Many also use details that would not meet the BMJ’s policy on patients’ confidentiality. Dr Crippen, for example, keeps a work diary that details consultations with noteworthy patients.

Ben Goldacre says that blogs are popular because they are more honest than other media: “It is hard to get away with misrepresenting stuff when the original source is but a click away. “I see it as a way of making conversation public—what is good about it is you get unmediated expertise. In the old days, you had to rely on a journalist to tell you what, for example, Iain Chalmers, told them. I think journalists were often really bad at this. On a blog, there he is. In the press it’s hard to know what is true. But with blogs people can link directly to the original source—this never happens in a newspaper.”

He complains that newspapers will also plagiarise blogs without giving credit, whereas blogs will refer and link to a person’s site. And on an online blog people can make instant comments, verifying a story or adding more information, whereas “in newspapers the comment is published a few days after the original article, when everyone else has moved on,” says Dr Goldacre.
Professor Colquhoun was switched on to the power of blogs after fighting a successful campaign to halt the proposed merger of Imperial College and University College London. “Everyone was unhappy about it but said it was a ‘done deal’ and could not be stopped. As soon as I started a blog support came flooding in, and it was possible to publish raw, unfiltered information instantly. It took only five weeks after starting the blog to defeat the whole daft idea, and that made me realise the amazing power of the web.”

After peace descended on UCL Professor Colquhoun found he was addicted, and he started to publish opinions on quackery and also on politics, religion, and education. “It slowly dawned on me that all these pages were closely related, [were] just different aspects of ‘endarkenment’ thinking, and the pages got too big to load quickly, so they are now all supplanted by two proper blogs” (including DC’s Improbable Science at http://dscience.net/).

Professor Colquhoun says he still gets an “enormous” amount of enjoyment from blogs. “I think they have really had some success in spreading public understanding of science and even in influencing public affairs (firstly with the merger and more recently with withdrawal of NHS funding for homeopathy). My own research is on the stochastic properties of single ion channels. I love it, but it is specialist and of zero interest to the public. So it’s fun to talk about things that do interest the public. It’s also fun to be able to influence politicians and vice chancellors, though that is rather harder.”

He says that before blogs the ordinary academic had no chance to influence anything much, other than by voting every five years. Now—with a little technical expertise—“they can post stuff for the world to see while sitting in front of the TV or even on a hilltop.” Blogs are also easy and cheap to produce—many blog hosts are free.

What turns off many would be users is the feeling that the blogosphere is a wild west of crackpot opinion-mongers. How do you determine the relative “value” of a medical blog? Ben Goldacre says that it is easy to sift through the huge choice of medical blogs, building up a bank of trusted sites and following trails to new ones.

He says, “I’m a 33 year old doctor, and I most enjoy reading narrow interest magazines. A BMJ editorial is always going to be more interesting to me than a Times editorial, a Nature article more than a New Scientist feature. The http://science.reddit.com site [a ranking of science writing that is posted and voted on by users] is consistently brilliant, much better than anything in the newspapers.” Blogs also offer users “grand rounds”—informal syndication of the best from other blogs. For example, a group of blogs will take it in turns to host a paediatric grand round, rounding up the best of that week’s blog entries related to paediatrics.

Professor Colquhoun adds: “Blogs are an enormous step towards real democracy, though the price for that is that every madman and quack can do the same. Indeed, that is what makes it so important for people with knowledge, expertise, and honesty to fight back and draw a line in the sand at the tide of nonsense that engulfs us. The papers don’t fulfil that role at all well—and in fact often exacerbate it.”

Rebecca Coombes is a journalist, London rcoombes@bmjgroup.com

**MEDICINE AND THE MEDIA**

**Patients’ blogs: do doctors have anything to fear?**

Blogs written by parents about their sick children’s care can be beneficial if handled sensitively. **Matthew Hurley** and **Craig Smith** point out the pitfalls

In recent months we have had very different experiences of parents using blogs. One family used a blog simply to update family and friends overseas about their extremely premature baby. It contained a daily record of events, including details of procedures and the names of staff looking after their baby. In another blog the parents of a baby with rare congenital abnormalities used it to keep detailed records of medical care and decisions, including discussions and disagreements with different medical and nursing staff. Both blogs initially caused some concern among staff.

The phenomenon of parents’ blogs may have a unique association with paediatric and neonatal practice. It is common practice for parents to take photographs of their babies to log their progress. Electronic dissemination makes sharing these experiences easier, and for many the blog is simply the modern photograph album or memory box. Keeping a blog can be beneficial to parents: it lightens the burden of daily telephone contact and provides written support when others reply to the site. Many parents already publish their experiences on conventional websites in the hope of helping others. Such altruistic blogs include entries on charity affiliated websites, which can be used to publicise a particular illness by attracting the media to an individual’s story. This medium may also lend itself to whistleblowing in the public interest.

Blogs can be a useful source of information for patients. Parents go to the internet for information during diagnosis and treatment of their child’s illness. Blogs narrate an individual’s experience that may not be representative. Parents intent on leading care decisions, in an attempt to achieve the best possible care for
their child, could use their own or other blogs as a novel way of meeting this objective. This information must be viewed with caution, but it can also encourage discussion and learning. At our hospital the parent can take a “prescription” for information from the community paediatrician to the patient information library, where a specialist librarian is available to direct the family to reliable resources.

Reading a family’s experience of an illness and the care given can provide clinicians with a valuable insight into parents’ understanding and help identify elements of the care pathway that need improvement. The temptation to contribute to a patient’s online blog needs careful consideration. Employees who write about their work on blogs have been “doved”—that is, they have lost their jobs through expressing their views in a blog. Instead, more effort should be taken to improve opportunities of communication and the elements of care under discussion.

Blogging has legal implications. Healthcare professionals feel vulnerable about the publication of unedited material and opinion in real time. They may also be uneasy about parents who keep online diaries that may be used as evidence in complaints or legal proceedings. In our experience, many parents already keep a written journal and photographs logging their baby’s journey. An identical electronic version would have no additional legal ramifications.

If difficulties arise during care and the details are published, potential exists for the parent-doctor relationship to be compromised. Blogging, as a form of publishing, is subject to the laws governing defamation, which aim to protect a person or an organisation’s reputation from harm. If you think that you are the subject of an untruthful, unwarranted, or mistaken attack on your reputation, you may have been libelled. Healthcare professionals may feel that a blog misinterprets a sequence of events or, even worse, calls into question their competence or professionalism, publicising this to other parents and staff. Healthcare staff must then decide whether they wish to pursue defamation.

If pursued, the publisher (the internet service provider) may claim “innocent dissemination,” stating that they did not know that any published statement was defamatory. However, the Defamation Act 1996 makes provision for publishing an apology and paying costs. The internet publisher should have a “notice and take down policy,” whereby offending material may be withdrawn from public access.

There is also a risk that blogs may compromise the right of confidentiality of other patients on the ward or their parents. The legal and ethical protection of confidentiality is underpinned by the Data Protection Act and by the General Medical Council. Parents should be encouraged to write in a way that doesn’t identify individuals. Simple guidance for parents and professionals needs to be developed.

We support the use of blogs by families. Indeed, we aim to provide internet access for families in the near future to facilitate this. However, we recognise the vulnerability of everyone involved and aim to give guidance to parents and staff about parents’ and patients’ blogs.

Matthew Hurley is senior house officer, paediatric intensive care unit, Queen’s Medical Centre, Nottingham hurleymm@doctors.org.uk
Craig Smith is consultant neonatologist, neonatal intensive care unit, Nottingham University Hospitals craig.smith@nuh.nhs.uk

WHAT’S ON BMJ.COM

The dangers of attacking disease programmes for developing countries

Roger England has launched yet another broadside attack on programmes for priority diseases in poor countries (BMJ 2007;335:565 and 2007;334:346). In his latest Personal View, he claims that “disease specific global programmes [are] not the way to help Africa,” instead that they cause “big problems for recipients,” and that money for HIV/AIDS is “the worst.” He claims that off-budget money leads to distortions; that there are duplications of plans, operations, and monitoring; and that priority disease programmes are neither cost effective nor sustainable.

His evidence that little is being achieved is one statistic: HIV prophylaxis is reaching only 9% (actually it is 11%) of pregnancies of HIV positive women. He blames the warped prioritisation of disease programmes on international lobby groups from rich countries. England’s prescription for change says that governments must stop funding global programmes that do not go through countries’ planning and budgeting processes; the Global Fund to Fight AIDS, Tuberculosis, and Malaria must disband and be reconstituted as a global health fund; countries must reform their systems and outsource service provision from the government to the private sector; and everyone should drop the millennium development goals because they are more trouble than they are worth.

The evidence on hand rebuts or at least moderates many of England’s claims and recommendations.

Priority disease programmes have shown considerable progress in a relatively short period of time. Currently, the Global Fund contributes two thirds of international funding for tuberculosis and malaria, and about 20% of global resources for HIV/AIDS, for example. In its short life it has funded programmes that have already saved more than 1.8 million lives; provided antiretroviral treatment to 770 000 people; distributed more than 18 million bed nets; and treated two million new patients with tuberculosis.

Attacking priority diseases programmes and calling for the dismantling of the Global Fund and decommissioning of the millennium development goals is a prescription for returning global health and priority diseases to the backwater of broken promises and failed development.

Instead of criticising the movement and activities that form the leading edge of the driving wedge for global health reform, England, and more particularly planners, donors, and developing countries, should focus on rationalising increasingly robust priority diseases programmes so that they work laterally to strengthen health systems.

By all means, these same policy makers should work much more vigorously to provide sustainable financing for health in quantities sufficient for expanding human resources for health and strengthening the health systems that deliver prevention, treatment, and care for all health needs. We realise that integration of priority diseases programmes in revitalised health systems in the long term is important. But we also know that suspending these programmes prematurely will sacrifice millions on the altar of a health systems theory that made little progress since Alma Ata until the AIDS movement became the high speed engine on the train of health systems development.

Simon Collins, treatment advocate, HIV i-Base, London, and International Treatment Preparedness Coalition
Brook K Baker is Northeastern University School of Law, Health Global Access Project
Gregg Gonzales AIDS and Rights Alliance for Southern Africa
Marco Gomes Global Youth Coalition on HIV/AIDS
Contact S Collins simon.collins@i-base.org.uk

This is a short version of a rapid response on bmj.com. The full version is at www.bmj.com/cgi/eletters/335/7619/565#176912.
YANKEE DOODLING

Douglas Kamerow

Wham, bam, thank you CAM

Alternative medicine is wildly popular in the United States, but what are we supposed to do about it?

I got a phone call the other day from a man asking whether I did “alternative” medicine. When I told him that I wasn’t in regular practice, he asked for a referral to someone who could provide this type of care. It made me think.

Complementary and alternative medicine (CAM) comprises a diverse group of treatments, ranging from symptomatic interventions to be used in conjunction with traditional therapies—therapeutic touch or meditation—to unique treatments meant to replace conventional chemotherapy or surgery. CAM includes complex and longstanding fields of study, such as acupuncture, ayurvedic medicine, and homoeopathy, but can also be as straightforward as taking a specific dietary supplement to lower blood pressure or blood lipid concentrations.

Americans love CAM. Over a third of them report having used some form of CAM therapy in the previous 12 months, and the use is increasing every year. Leading CAM therapies include natural products (supplements and herbal medicines and so on), meditation, chiropractic, and massage. Symptoms most commonly treated with CAM therapies include musculoskeletal, respiratory, and psychological symptoms.

It’s a huge business: Americans spend at least $50bn (£25bn; €36bn) a year on CAM therapies. An increasing amount of this care is covered by US health insurance schemes, although generally this applies only to the more accepted CAM treatments, such as acupuncture and chiropractic. About a third to a half of spending on CAM is paid out of patients’ pockets, more than we pay directly for hospitalisations.

Despite all this many Americans don’t like to talk to their doctors about the CAM treatments they are using. Only about a third to a half of patients who use CAM report discussing this with their doctor. Their reasons vary from thinking that doctors will not be supportive to saying that it is not important for doctors to know. That’s a potential problem, given the documented interactions between some natural products and conventional drugs. Surveys in the US find that doctors rarely ask about use of CAM products, even though they admit they need to know more about them.

With all of this activity, it would be nice to know which CAM treatments work and which don’t. A number of Cochrane reviews have looked at CAM treatments, and the US Agency for Healthcare Research and Quality has commissioned around 20 evidence reports—systematic reviews—on CAM therapies. The UK’s National Institute for Health and Clinical Excellence (NICE) has explicitly avoided assessing CAM, however, despite calls for it to do so (BMJ 2007;334:506 and BMJ 2007;334:507).

In addition, in response to a mandate from Congress, the US National Institutes of Health created the National Center for Complementary and Alternative Medicine in 1999. Its mission is to support rigorous research into CAM and to disseminate its results. This research ranges from large randomised controlled trials of CAM products to basic science research to elucidate physiological explanations for CAM therapies such as acupuncture and ayurvedic medicine. The centre has spent hundreds of millions of dollars investigating CAM products and treatments.

So why don’t we know more than we do about what works and what doesn’t? Part of the explanation is the huge number and heterogeneity of CAM interventions. Only a small number of the most promising treatments have so far been rigorously tested. Part of the problem is the nature of CAM treatments: they can be hard to quantify and hard to specify, and often they don’t lend themselves to standard research techniques such as placebo controlled trials.

Furthermore, once research is done, it is often hard to assess its quality. Paul Shekelle and colleagues have written about the difficulties of systematically reviewing CAM studies (Annals of Internal Medicine 2005;142:1042-7). The challenges include publication, expectation, and other biases; difficulty in locating the literature; treatment variability; variability in use of placebo or sham treatment; and dealing with rare but serious adverse events.

Critics say that CAM doesn’t deserve a place at the table—that enough time has passed and enough research has been done to show whether any of these interventions are safe and effective. The fact that unequivocal success stories are few indicates only that the treatments are placebo and expectation effects masquerading as medicine, they say. And yet so many people use them and seem to derive benefit, it seems a shame to lump them all together and throw them out.

I think a sensible approach is, firstly, for doctors to inquire of patients what non-traditional treatments they are using, both for conditions that the doctor knows about and is treating and for others that have not been dealt with. This will at least allow discussion and investigation of possible adverse interactions. Secondly, doctors should discuss truly complementary symptomatic CAM treatments—for chronic pain, allergies, or the like—so that their scientific basis can be investigated and understood by the patient and the doctor, if possible. Thirdly, for alternative treatments for serious or life threatening diseases such as cancer, doctors should assess the scientific evidence for the treatment and try to understand the range of benefit the patient expects to receive from it.

Although the US seems to lag behind the United Kingdom, we all need to pay more attention to the CAM treatments that our patients are seeking out and are willing to pay for and to the evidence behind their effectiveness. Douglas Kamerow, former US assistant surgeon general, is a BMJ associate editor dkamerow@bmj.com

So many people use alternative treatments and seem to derive benefit, it seems a shame to lump them all together and throw them out.

Douglas Kamerow, former US assistant surgeon general, is a BMJ associate editor dkamerow@bmj.com

29 SEPTEMBER 2007 | VOLUME 335
Use of process measures to monitor the quality of clinical practice

Outcomes of care are a blunt instrument for judging performance and should be replaced, say Richard J Lilford, Celia A Brown, and Jon Nicholl

Healthcare organisations are increasingly scrutinised by external agencies, such as the Health Care Commission in England and Medicare in the Unites States. Such agencies increasingly concern themselves with the quality of care and not just measures of throughput, such as waiting times and the average length of hospital stay. Measures of clinical quality are also likely to be used increasingly to monitor the performance of individual doctors.1 But how should quality be measured? The intuitive response is to measure the outcomes of care—after all, patients use the service to improve their health outcomes. We argue that this beguiling solution has serious disadvantages because of the poor correlation between outcome and quality and that use of outcome as a proxy for quality is a greater problem when the data are used for some purposes than for others.

Purpose of measurement

Data on quality can be used either for internal quality improvement or for external reporting. In the first scenario, data are collected by an organisation or individual for internal audit in the spirit of continuous improvement (quality circles, total quality management, plan do act, Kaizen, etc). In the second scenario, monitoring is imposed externally by health service funders for purposes of accountability (performance management). When results lie above or below some predefined threshold, funders may use the data to prompt further investigation in a completely non-pejorative manner. Alternatively, they may use data as the basis for sanction or reward. For example, hospitals may be given ratings that determine managerial freedoms and financial reward or a doctor may be suspended. We shall refer to use of data for sanction or reward as data for judgment. It is such use that is particularly problematic.

Outcomes and quality

The main disadvantage of measuring outcomes arises from the low signal to noise ratio: outcomes are likely to be affected by factors other than the quality of care. A recent systematic review showed that, although statistically significant, the correlation between the quality of clinical practice and hospital mortality is low2 and hence mortality is neither a sensitive nor a specific test for quality. Modelling shows that big differences in the quality of care are likely to be lost in mortality statistics3 and that over half of the institutions with the worst quality of care are likely to have mortality in the normal range and vice versa.4 The situation may be worse at the community level.5

It is a myth that the problem of poor correlation between quality and outcomes can be solved by statistical adjustment for risk (the risk adjustment fallacy).6 Risk adjustment does not remove the problems of bias in rankings for two reasons:

Firstly, risk adjustment cannot allow for case mix variables that have not been measured (perhaps because they are unknown) and are therefore omitted from the statistical model. Nor can it allow for differences in definitions (or in how the same definitions are applied) to either numerators or denominators. For instance, differences in discharge policies (perhaps influenced by availability of a local hospice) will affect the types of patients included in the statistics.

Secondly, risk adjustment is sensitive to modelling assumptions. Adjustment may even increase bias if the risk associated with the risk factor is not constant across groups being compared.7 8 For example, the effect of age on mortality may be greater in some groups (such as those from low socioeconomic backgrounds) than in others. If this is the case risk adjustment will under-adjust for groups in which age has the largest effect. The predicted mortality will be lower than the observed mortality and the playing field is tilted against clinicians or institutions in places where the age effect is greatest.

The problems of risk adjustment do not just apply to mortality but also to other outcomes, such as surgical site infections, for which the definition varies widely from place to place. Using surrogate outcomes, such as the proportion of diabetic patients whose measure of glucose control exceeds some threshold, brings in further confounding variables, such as systematic differences in patients’ willingness to adhere to treatment. Even using patient satisfaction to rank individuals or institutions for humane care is potentially misleading since the results may be confounded by systematic differences in expectations.9

There may be some topics where the signal to noise ratio is much better than in the examples cited above and hence where a sizeable portion of the variance in outcome is made up of variance in quality. If such examples exist, they are likely to arise among the most technically demanding services such as paediatric cardiac surgery. Claims and counter claims have been made about the role of outcome monitoring for coronary artery bypass surgery.10 We suspect that even in these topics case selection and other differences between institutions have the major role. We therefore believe those who wish to use such outcomes for performance management within an
accountability framework must first prove that they are strongly correlated (not just statistically associated) with quality.

**Using outcomes for sanction or reward**

With some possible exceptions, outcomes are clearly neither sensitive nor specific measures of quality. Managers and clinicians therefore quite properly distrust them. This can induce perverse incentives—staff apply their ingenuity to altering or disproving the figures rather than tackling quality or safety, patients are nudged into more severe prognostic categories, treatment may be targeted at patients with the best prognosis (who are often those with the least capacity to benefit), and there are even cases where statutory data have been altered.11,12

The problem that outcome data are poor barometers of clinical quality is viciously confounded by both their inability to discriminate between good and poor performers13 and the lack of information they convey about how improvements should be made. In education, for example, it is now standard practice to include a comment and not just a grade when assessing an essay or assignment. Using outcomes to trigger sanctions or rewards may induce a sense of shame or institutional stigmatization—the feeling of diminished status that comes of being branded bad without being told what the problem is.

When outcomes are used to judge the performance of individual clinicians further problems arise. Firstly, the results are less precise than they are at institutional level. Secondly, outcomes synthesize all of the processes received by the patient and therefore reflect the activities of many clinicians and support services.

**Process: an alternative measure**

Measures of clinical process have many advantages over outcomes. These advantages are particularly important if policy makers insist on using data for judgment. Clearly, the processes selected for scrutiny must comprise accepted and scientifically valid tenets of clinical care: do patients with a fractured neck of the femur get surgery within 24 hours? Are patients on ventilation nursed in a semi-prone position? Do clinicians monitor respiratory rate on the acute medical wards and, if so, do they respond promptly to signs of deterioration?

Such measures are not a panacea. The measures themselves must be valid and important. Furthermore, process measures are not immune from case mix bias; sicker patients challenge the system more than those who are not so sick, so the playing field is tilted against those who care for more vulnerable patients. Nevertheless, we believe that process measures have four fundamental advantages over outcomes:

- **Reduction of case mix bias**—Using opportunity for error rather than the number of patients treated as the denominator reduces the confounding that arises when one clinician or institution cares for sicker patients than another.14 This is because sicker patients present more opportunities for clinical process errors (of either omission or commission). Expressing errors as a function of opportunities for those errors adjusts (at least in part) for case mix bias. This method cannot be used when outcomes are assessed because the patient is the smallest possible unit of aggregation under these circumstances.

- **Lack of stigma**—The message is “improve X,” not “you are bad.” For this reason they are less likely to prompt perverse solutions. Arguably it is easier and more natural to improve the care process than to try to discredit the measure (see below).

- **Prompt wider action**—Process measures encourage action from all organisations or individuals with room for improvement, not just a small proportion of outliers. Shifting the whole distribution will achieve a larger health gain than simply improving the performance of those in the bottom tail, as the figure shows. Assuming a normal distribution in quality, a shift of 10% would result in a health gain of 10%. However, improving the performance of the bottom 10% would produce a gain of 7.2%, even if this threshold distinguished perfectly between good and poorly performing units. Furthermore, organisations do not fail simultaneously across all dimensions of safety and quality. Rather they have particular strengths and weaknesses and improvement efforts can be targeted where they are needed: there is no need to produce a summary measure across criteria. In fact, we found no correlation between adherence to various evidence based quality criteria in 20 randomly selected UK maternity units.15 Thus, a hospital with above average recorded outcomes is still likely to have room for improvement in many aspects of care.

- **Useful for delayed events**—Process measures are more useful than outcomes when the contingent adverse event is markedly delayed (such as failing to monitor patients with diabetes for proteinuria or to administer anti-D immunoglobulin when a rhesus negative woman gives birth to a rhesus positive baby).

**Selecting and measuring clinical processes**

Process standards used in performance management should be valid in that they must either be self evident measures of quality or be evidence based. However, validity is not sufficient—the standards must also be genuinely important to health care. This is because the opportunity cost of improving some processes may exceed the contingent gains.16 Worse, healthcare providers may put their efforts into the monitored processes at the expense of those that are not monitored.17 One way to ameliorate this effect may be to elicit clinical
are a better method of judgment. However, process is not a specific measure of quality, process measures are implicit measures of the association is low. Outcome data can also be used (such as mortality) may be traced to a problem in the water supply. Lastly, the public are entitled to have access to outcome data, although such outcomes should always be published with a proper warning about the limitations.

Is performance management effective?

Where outcomes are a specific measure of quality, externally imposed performance management by outcome may be effective. Collection of outcome data for cardiac surgery in the UK seems to have raised standards, although debate continues about whether the observed improvements exceed the secular trend.10

In the more common scenario where outcomes are not a specific measure of quality, process measures are a better method of judgment. However, process is expensive to measure as it currently requires access to patients’ case notes. Evaluating case notes is time intensive and requires staff with clinical expertise. Electronic patients records and an increase in coded information in these records should make monitoring easier.

The cost of obtaining process measurements (and the contingent action) needs to be compared to the value (in terms of health benefit) of the improvement in quality that results from providers’ responses to initial measurements. Although much of the evidence of effectiveness relates to bottom-up improvement programmes,24 there is also empirical support for the effectiveness of top-down performance management using process measures.23 24

Are outcome measures obsolete?

Although process measures are the most suitable tool for performance management, measurement of outcomes remains important. Outcomes are useful for research, particularly for generating hypotheses. Here, simply finding an association between a variable (such as staff-patient ratios) and outcome (such as mortality) may be sufficient to prompt investigation, even when the strength of the association is low. Outcome data can also be used as a form of process control, such that institutions with abrupt changes in outcome or whose outcomes deviate by a large amount (three standard deviations or more is a sensible threshold25) can be further investigated. For example, an outbreak of hospital acquired infection may be traced to a problem in the water supply. Lastly, the public are entitled to have access to outcome data, although such outcomes should always be published with a proper warning about the limitations.

Outcomes are useful for research, particularly for generating hypotheses

We thank the referees for helpful comments.

Contributors and sources: This paper is the result of a synthesis of prolonged writing, review, and consultation with experts in the field. RJL has had many opportunities to debate and test the argument presented here, most notably as a participant at numerous Pennyhill Anglo-American health summits. RJL conceived the article, which was subsequently drafted by RJL, CAB, and JN. All three authors approved the final manuscript. RJL is the guarantor.

Competing interests: None declared.

Provenance and peer review: Not commissioned, externally peer reviewed.

Cancer risk among users of oral contraceptives: cohort data from the Royal College of General Practitioner’s oral contraception study

Philip C Hannaford, professor,¹ Sivasubramaniam Selvaraj, research fellow,² Alison M Elliott, senior research fellow,¹ Valerie Angus, data manager,³ Lisa Iversen, research fellow,¹ Amanda J Lee, professor of medical statistics¹

ABSTRACT
Objective To examine the absolute risks or benefits on cancer associated with oral contraception, using incident data.
Design Inception cohort study.
Setting Royal College of General Practitioners’ oral contraception study.
Participants Directly standardised data from the Royal College of General Practitioners’ oral contraception study.
Main outcome measures Adjusted relative risks between never and ever users of oral contraceptives for different types of cancer, main gynaecological cancers combined, and any cancer. Standardisation variables were age, smoking, parity, social class, and (for the general practitioner observation dataset) hormone replacement therapy. Subgroup analyses examined whether the relative risks changed with user characteristics, duration of oral contraception usage, and time since last use of oral contraception.
Results The main dataset contained about 339 000 woman years of observation for never users and 744 000 woman years for ever users. Compared with never users ever users had statistically significant lower rates of cancers of the large bowel or rectum, uterine body, and ovaries, tumours of unknown site, and other malignancies; main gynaecological cancers combined; and any cancer. The relative risk for any cancer in the smaller general practitioner observation dataset was not significantly reduced. Statistically significant trends of increasing risk of cervical and central nervous system or pituitary cancer, and decreasing risk of uterine body and ovarian malignancies, were seen with increasing duration of oral contraceptive use. Reduced relative risk estimates were observed for ovarian and uterine body cancer many years after stopping oral contraception, although some were not statistically significant. The estimated absolute rate reduction of any cancer among ever users was 45 or 10 per 100 000 woman years, depending on whether the main or general practitioner observation dataset was used.
Conclusion In this UK cohort, oral contraception was not associated with an overall increased risk of cancer; indeed it may even produce a net public health gain. The balance of cancer risks and benefits, however, may vary internationally, depending on patterns of oral contraception usage and the incidence of different cancers.

INTRODUCTION
Since the introduction of oral contraception in the early 1960s more than 300 million women are thought to have used it,¹ often for prolonged periods and at a time of good health. Many studies have examined the potential association between oral contraception and cancer. The evidence suggests that current users of combined oral contraceptives have an increased risk of cancer of the breast, cervix, and liver compared with non-users.¹⁻⁴ The risks of breast and cervical cancer decline after stopping oral contraception, returning to that of non-users within about 10 years.²⁻³ Current users of combined oral contraceptives, however, have a reduced risk of cancer of the endometrium,¹⁴ ovaries,¹⁴ and, possibly, colorectum.¹⁻⁵ The benefits for ovarian and endometrial cancers seem to persist for many years after stopping oral contraception, perhaps more than 15 years.¹⁻⁴ The long term cancer benefits might counter the short term harmful ones if they persist into the age when most malignancies become common in women—50 years or more.

Cohort studies are particularly useful for investigating the overall balance of risks and benefits associated with an exposure. Two large cohort studies reported on the overall risk of death from cancer among ever and never users of oral contraception; neither found significant differences between the groups.⁷⁻⁸ Although this was reassuring for fatal cancers further exploration of the overall balance of cancers is needed using incident data. A Norwegian cohort study found no significant association between oral contraceptive use and the combined risk of breast, endometrial, and ovarian cancer.⁹ A neutral balance of invasive genital cancers among ever and never users of oral contraception was found in the Royal College of General Practitioners’ oral contraception study in the late 1980s.⁹ Recently the Oxford/Family Planning Association contraceptive study found a significantly reduced risk of
gynaecological cancers combined among ever users of oral contraceptives compared with never users. We used data from the oral contraception study to test the hypothesis that, compared with never users, ever users of oral contraception have a reduced overall risk of cancer, an effect that is strongest in women aged 40-60.

METHODS
The Royal College of General Practitioners’ oral contraception study began in May 1968. Over a 14 month period 1400 general practitioners throughout the United Kingdom recruited about 23 000 women who were using oral contraceptives and 23 000 women who had never used them. The mean age at recruitment was 29 (standard deviation 6.6). All the women were married or living in a stable relationship and most were white. Baseline information collected included smoking habits, social class (based on husband’s occupation), parity, and important medical history. After recruitment the general practitioners supplied information every six months about any hormonal preparations prescribed, any pregnancies and their outcome, all new episodes of illness (including cancer), and any surgery in women still under their observation. Women remained under follow-up by their general practitioner until they left the area of the recruiting doctor (about 56% of total cohort), their doctor left the study (13%), they obtained their contraceptives from a source other than the general practice (3%), they died (2%), or the study stopped follow-up by general practitioners (at the end of 1996, 26%).

In the mid-1970s three quarters of the original cohort was flagged at National Health Service central registries in Scotland and England so that subsequent cancers and deaths could be reported to the study, even if women were no longer under follow-up by their general practitioner. The remaining 24% of women could not be flagged because they or their doctor left the study before flagging started.

Two datasets were compiled. In both, women not flagged were included up until they were lost to follow-up (figure). In addition, the main dataset included information up to the date of the first relevant cancer or December 2004 (whichever came first) for flagged women still under observation by their doctors when such follow-up stopped in 1996, for flagged women lost to the study before 1996 who were aged 38 or more at the time of loss, and for flagged ever users lost to the study before 1996 who were younger than 38 at the time of loss. We excluded, from the time of loss, flagged never users younger than 38 and lost to general practitioner follow-up before 1996 because we did not know whether they subsequently started using oral contraceptives. We assumed that older never users were unlikely to have started oral contraceptives because 91% of women in the study who used oral contraceptives were unlikely to have started oral contraceptives because 91% of women in the study who used oral contraception began their use before the age of 38.

Two datasets were compiled. In both, women not flagged were included up until they were lost to follow-up (figure). In addition, the main dataset included information up to the date of the first relevant cancer or December 2004 (whichever came first) for flagged women still under observation by their doctors when such follow-up stopped in 1996, for flagged women lost to the study before 1996 who were aged 38 or more at the time of loss, and for flagged ever users lost to the study before 1996 who were younger than 38 at the time of loss. We excluded, from the time of loss, flagged never users younger than 38 and lost to general practitioner follow-up before 1996 because we did not know whether they subsequently started using oral contraceptives. We assumed that older never users were unlikely to have started oral contraceptives because 91% of women in the study who used oral contraceptives were unlikely to have started oral contraceptives because 91% of women in the study who used oral contraceptives.
contraceptives started to do so before age 38. This threshold was chosen as a balance between maximising the amount of data available for analysis and minimising the risk of misclassification of contraceptive status. Never users in the main dataset therefore were women who were known, or assumed, to have never used oral contraceptives.

The general practitioner observation dataset included cancers, periods of observation, and other relevant information obtained while women were under observation by their doctors up to the point of their being lost to follow-up, the first relevant cancer, or December 1996, when all observations by doctors stopped (whichever came first). This dataset had comprehensive information about type and duration of oral contraceptives used, information that could not be updated once women left observation. It also contained information about use of hormone replacement therapy while under general practitioner follow-up.

The main dataset had the largest amount of data and so provided the most precise risk estimates. In this paper we present cancer rates for ever and never users from both the main and general practitioner observation datasets; rates of any cancer in different age, parity, smoking, and social class subgroups of women in the main dataset; and cancer rates by duration and time since last use of oral contraceptives, using the general practitioner observation dataset (since complete information about this variable was only available in this dataset).

The cancers were coded using the international classification of diseases, eighth revision. They were recorded one event and coded it as cancer site (codes 153 and 154), gallbladder or liver (155 and 156), lung (162), melanoma (172), breast (174), invasive cervix (180), uterine body (182), ovary (183), central nervous system or pituitary (191 and 1943), site unknown (199), and other cancers (any event with a code between 140 and 209 not already mentioned; main gynaecological cancers combined (180, 182, and 183); and any cancer (140-209). Most cancers in the main dataset were notified by the central registries only (2342/3877 (60%) of any cancers). Of the 1651 any cancers in the general practitioner observation dataset, 840 (50.9%) were notified by the doctor, 116 (7.0%) by the central registries, and 695 (42.1%) by both. If a discrepancy occurred between sources we sought clarification from the doctor if possible. In 13 cases the date of cancer occurrence differed by more than three months and in 312 between one and three months. In each case we used the information notified by the doctor. In 30 cases the ICD-8 codes differed between the two sources. When the discrepancy could not be reconciled, the doctor notified information took precedence (24 cancers). On 19 occasions more than one cancer was reported for the same date and we were unable to check the original records. In these instances we recorded one event and coded it as cancer site unspecified.

**Table 1 | Characteristics of women who ever or never used oral contraceptives**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No (%) of ever users of oral contraceptives</th>
<th>No (%) of never users of oral contraceptives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at recruitment (years):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>18 305 (63.6)</td>
<td>8854 (51.5)</td>
</tr>
<tr>
<td>30-39</td>
<td>8690 (30.2)</td>
<td>6579 (38.3)</td>
</tr>
<tr>
<td>40-49</td>
<td>1744 (6.1)</td>
<td>1724 (10.0)</td>
</tr>
<tr>
<td>50-59</td>
<td>23 (0.1)</td>
<td>31 (0.2)</td>
</tr>
<tr>
<td>Smoking at recruitment (cigarettes per day):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>15 054 (52.3)</td>
<td>10 371 (60.3)</td>
</tr>
<tr>
<td>1-14</td>
<td>7986 (27.8)</td>
<td>4164 (24.2)</td>
</tr>
<tr>
<td>≥15</td>
<td>5772 (19.9)</td>
<td>2653 (15.4)</td>
</tr>
<tr>
<td>Parity at recruitment:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4862 (16.9)</td>
<td>3458 (20.1)</td>
</tr>
<tr>
<td>1</td>
<td>6570 (22.8)</td>
<td>4465 (26.0)</td>
</tr>
<tr>
<td>2</td>
<td>9179 (31.9)</td>
<td>5472 (31.8)</td>
</tr>
<tr>
<td>≥3</td>
<td>8151 (28.3)</td>
<td>3793 (22.1)</td>
</tr>
<tr>
<td>Social class at recruitment:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-manual</td>
<td>10 347 (36.0)</td>
<td>6630 (38.6)</td>
</tr>
<tr>
<td>Manual</td>
<td>18 415 (64.0)</td>
<td>10 558 (61.4)</td>
</tr>
<tr>
<td>Never used hormone replacement therapy</td>
<td>25 056 (87.2)</td>
<td>15 453 (90.0)</td>
</tr>
<tr>
<td>Ever used hormone replacement therapy</td>
<td>3695 (12.9)</td>
<td>1716 (10.0)</td>
</tr>
</tbody>
</table>

Values for age, smoking, parity, and social class based on main dataset and for use of hormone replacement therapy on general practitioner observation dataset.
other cancer groups (since the woman remained at risk of having another type of cancer). When analysing the risk of any cancer we counted only the first cancer (and censored subsequent periods of observation). The total number of any cancer in the tables therefore is less than the sum of each cancer category given separately, as women could have contributed data to more than one category. When calculating 95% confidence intervals we assumed approximate normality for the log of estimated relative risks. We tested trends for duration and time since last use of oral contraception using the log-linear trend test, by including them as metric explanatory variables with even spaced levels. For clarity of presentation we give only the standardised rates for analyses of the subgroup of duration and time since last use of oral contraception.

RESULTS

The main dataset contained about 744,000 woman years of observation for ever users of oral contraception and 339,000 woman years for never users. The corresponding values for the general practitioner observation dataset were 331,000 and 224,000 woman years. Compared with never users ever users tended to be younger, smokers, of high parity and manual social class at recruitment, and to have used hormone replacement therapy (table 1).

Using the main dataset ever users of oral contraception compared with never users had a statistically significant 12% reduction in the risk of any cancer (adjusted relative risk 0.88, 95% confidence interval 0.83 to 0.94, table 2). Statistically significant reductions were found in rates of cancer of the large bowel or rectum, uterine body and ovaries, as well as those of site unknown and “other.” Conversely, small, statistically non-significant increases were found in the risk of cancers of the lung, cervix, and central nervous system or pituitary. No material difference was found between groups for the most common cancer.

### Table 2 | Risk of cancer among ever and never users of oral contraceptives in main dataset and in general practitioner observation dataset

<table>
<thead>
<tr>
<th>Malignancies</th>
<th>ICD-8 code</th>
<th>Ever users</th>
<th></th>
<th>Never users</th>
<th></th>
<th>Relative risk† (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Observed rate (No of women)</td>
<td>Standardised rate</td>
<td>Observed rate (No of women)</td>
<td>Standardised rate</td>
<td></td>
</tr>
<tr>
<td>Main dataset:*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large bowel or rectum</td>
<td>153 and 154</td>
<td>24.65 (188)</td>
<td>26.01</td>
<td>38.56 (135)</td>
<td>36.10</td>
<td>0.72 (0.58 to 0.90)</td>
</tr>
<tr>
<td>Gallbladder or liver</td>
<td>155 and 156</td>
<td>1.83 (14)</td>
<td>1.99</td>
<td>3.70 (13)</td>
<td>3.62</td>
<td>0.55 (0.26 to 1.17)</td>
</tr>
<tr>
<td>Lung</td>
<td>162</td>
<td>26.97 (206)</td>
<td>27.12</td>
<td>25.94 (91)</td>
<td>25.77</td>
<td>1.05 (0.82 to 1.35)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>172</td>
<td>12.58 (96)</td>
<td>12.86</td>
<td>14.28 (50)</td>
<td>13.99</td>
<td>0.92 (0.65 to 1.29)</td>
</tr>
<tr>
<td>Breast</td>
<td>174</td>
<td>117.79 (891)</td>
<td>121.53</td>
<td>129.31 (448)</td>
<td>124.20</td>
<td>0.98 (0.87 to 1.10)</td>
</tr>
<tr>
<td>Invasive cervix</td>
<td>180</td>
<td>15.48 (118)</td>
<td>14.94</td>
<td>10.28 (36)</td>
<td>11.19</td>
<td>1.33 (0.92 to 1.94)</td>
</tr>
<tr>
<td>Uterine body</td>
<td>182</td>
<td>10.61 (81)</td>
<td>11.30</td>
<td>21.41 (75)</td>
<td>19.53</td>
<td>0.58 (0.42 to 0.79)</td>
</tr>
<tr>
<td>Ovary</td>
<td>183</td>
<td>12.57 (96)</td>
<td>13.23</td>
<td>26.54 (93)</td>
<td>26.66</td>
<td>0.54 (0.40 to 0.71)</td>
</tr>
<tr>
<td>Central nervous system or pituitary</td>
<td>191, 1943</td>
<td>4.45 (34)</td>
<td>4.79</td>
<td>4.27 (15)</td>
<td>3.56</td>
<td>1.34 (0.73 to 2.47)</td>
</tr>
<tr>
<td>Site unknown</td>
<td>199</td>
<td>7.20 (55)</td>
<td>7.22</td>
<td>12.54 (44)</td>
<td>11.34</td>
<td>0.64 (0.43 to 0.95)</td>
</tr>
<tr>
<td>Other cancers</td>
<td></td>
<td>113.93 (863)</td>
<td>119.49</td>
<td>145.20 (504)</td>
<td>135.57</td>
<td>0.88 (0.79 to 0.98)</td>
</tr>
<tr>
<td>Main gynaecological</td>
<td>180, 182, 183</td>
<td>38.75 (295)</td>
<td>39.58</td>
<td>58.41 (204)</td>
<td>55.54</td>
<td>0.71 (0.60 to 0.85)</td>
</tr>
<tr>
<td>Any cancer</td>
<td>140-209</td>
<td>333.68 (2485)</td>
<td>344.91</td>
<td>410.20 (1392)</td>
<td>390.37</td>
<td>0.88 (0.83 to 0.94)</td>
</tr>
<tr>
<td>General practitioner observation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dataset‡:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large bowel or rectum</td>
<td>153 and 154</td>
<td>19.63 (66)</td>
<td>22.07</td>
<td>25.85 (59)</td>
<td>26.11</td>
<td>0.85 (0.59 to 1.20)</td>
</tr>
<tr>
<td>Gallbladder or liver</td>
<td>155 and 156</td>
<td>2.08 (7)</td>
<td>3.06</td>
<td>2.63 (6)</td>
<td>2.76</td>
<td>1.11 (0.37 to 3.30)</td>
</tr>
<tr>
<td>Lung</td>
<td>162</td>
<td>19.91 (67)</td>
<td>19.47</td>
<td>17.07 (39)</td>
<td>18.87</td>
<td>1.03 (0.70 to 1.53)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>172</td>
<td>14.57 (49)</td>
<td>15.26</td>
<td>14.90 (34)</td>
<td>14.81</td>
<td>1.03 (0.66 to 1.60)</td>
</tr>
<tr>
<td>Breast</td>
<td>174</td>
<td>100.68 (337)</td>
<td>108.12</td>
<td>111.46 (253)</td>
<td>105.96</td>
<td>1.02 (0.87 to 1.20)</td>
</tr>
<tr>
<td>Invasive cervix</td>
<td>180</td>
<td>21.44 (72)</td>
<td>20.78</td>
<td>13.15 (30)</td>
<td>13.94</td>
<td>1.49 (0.97 to 2.28)</td>
</tr>
<tr>
<td>Uterine body</td>
<td>182</td>
<td>6.24 (21)</td>
<td>6.24</td>
<td>15.33 (35)</td>
<td>13.27</td>
<td>0.47 (0.27 to 0.81)</td>
</tr>
<tr>
<td>Ovary</td>
<td>183</td>
<td>9.81 (33)</td>
<td>10.25</td>
<td>21.90 (50)</td>
<td>20.28</td>
<td>0.51 (0.33 to 0.78)</td>
</tr>
<tr>
<td>Central nervous system or pituitary</td>
<td>191, 1943</td>
<td>4.16 (14)</td>
<td>4.10</td>
<td>1.31 (3)</td>
<td>1.27</td>
<td>3.23 (0.93 to 11.24)</td>
</tr>
<tr>
<td>Site unknown</td>
<td>199</td>
<td>6.54 (22)</td>
<td>7.01</td>
<td>10.50 (24)</td>
<td>8.97</td>
<td>0.78 (0.44 to 1.39)</td>
</tr>
<tr>
<td>Other cancers</td>
<td></td>
<td>91.13 (305)</td>
<td>94.60</td>
<td>103.90 (236)</td>
<td>98.58</td>
<td>0.96 (0.81 to 1.14)</td>
</tr>
<tr>
<td>Main gynaecological</td>
<td>180, 182, 183</td>
<td>37.53 (126)</td>
<td>37.36</td>
<td>50.46 (115)</td>
<td>47.56</td>
<td>0.79 (0.61 to 1.01)</td>
</tr>
<tr>
<td>Any cancer</td>
<td>140-209</td>
<td>282.53 (936)</td>
<td>295.96</td>
<td>318.67 (715)</td>
<td>306.59</td>
<td>0.97 (0.88 to 1.06)</td>
</tr>
</tbody>
</table>

ICD-8=international classification of diseases, eighth revision.

Never users as baseline.

*Main dataset: standardised rate per 100,000 woman years, adjusted for age, parity, smoking, and social status.

†General practitioner observation dataset: standardised rate per 100,000 woman years, adjusted for age, parity, smoking, social status, and ever use of hormone replacement therapy.

The total population available in each dataset was used as the standard in each analysis. This, as well as allowing for different variables in each dataset, means that the results from the two datasets should not be compared directly.
breast cancer. Taken together there was a 29% reduced risk of the main gynaecological cancers combined.

The risk estimates in the smaller general practitioner observation dataset were less precise, with many of the relative risks losing their statistical significance, including that of any cancer (adjusted relative risk 0.97, 0.88 to 1.06, table 2). The reduced risk of cancer of the uterine body and ovaries among ever users, however, remained statistically significant, with main gynaecological cancers combined of borderline significance.

In both ever and never users of oral contraceptives the rate of any cancer increased with age and smoking (table 3). In all age groups except the youngest, ever users had a lower risk of any cancer than never users, with statistically significant lower risks found in women aged 30-39 and 50-59. Among all smoking and social class, and most parity, subgroups ever users of oral contraceptives had a reduced risk of any cancer in comparison with never users; in many cases the differences were statistically significant.

The median duration of oral contraceptive use in the study was 44 months (interquartile range 19 to 83 months, range 1 to 344 months). When all cancers were considered together, women who used oral contraceptives for more than eight years had a statistically significant increased risk of any cancer (adjusted relative risk 1.22, 1.07 to 1.39, table 4). Statistically significant increased risks among longer term (≥8 years) users were observed for cancers of the cervix (adjusted relative risk 2.73, 1.61 to 4.61) and central nervous system or pituitary (5.51, 1.38 to 22.05). Conversely, prolonged use of oral contraception was associated with a statistically significant reduced risk of ovarian cancer (0.38, 0.16 to 0.88). The trends of increasing rates of cervical and central nervous system or pituitary cancer, and decreasing risk of uterine body and ovarian malignancy, with longer durations of oral contraception use were all statistically significant.

Analysis of the data by time since last use of oral contraception suggests that the protective effect of oral contraception for ovarian cancer lasts for at least 15 years after stopping, with reduced (statistically non-significant) relative risks still seen after longer time intervals (table 5). All of the risk estimates for uterine body cancer were also below unity, although only that for current and recent use (<5 years after stopping) was statistically significant. The trends for other cancers were less consistent. None of the tests for trend for individual cancers with time since last use were statistically significant. A borderline statistical trend was seen of declining risk of main gynaecological cancers combined with longer time since last use (P=0.041), as the initially increased risk of cervical cancer among current and recent users of oral contraception disappeared with time.

**DISCUSSION**

In this UK cohort, oral contraception was not associated with an overall increased risk of cancer. Depending on which dataset was examined, our analyses suggest either a statistically significant 12% reduced risk of any cancer (main dataset) or a more modest, non-significant, 3% reduction (general practitioner observation dataset). In either case we found no evidence of a substantial increased risk of cancer overall. A major strength of the study was the ability to include more than a million woman years of observation, accumulated over 36 years. Virtually all of the women in the study are now post-menopausal, of an age when many cancers become common. This provided a large number of events for analysis. When we were able to compare cancers notified by both sources we found a high degree of agreement between general practitioner and central registry notifications. The data supplied by the central registries depend on the completeness and accuracy of national cancer registries. Although a small proportion of cancers are likely to have been missing or wrong, there is no reason to suspect that systematic differences occurred between oral contraceptive groups.

We were able to adjust for the potentially important confounders of age, smoking, social class, parity, and (for the general practitioner observation dataset) use of hormone replacement therapy. In general the adjustments made little difference to the unadjusted rates. Although the smoking data used were those collected at study recruitment, any bias would tend to underestimate the effects of smoking. Furthermore, a study of a subset of women who completed a health survey in the mid-1990s produced virtually identical risk estimates for myocardial infarction
associated with oral contraceptive use based on
updated smoking data as those based on information
at recruitment.14 We did not adjust for differences in
hysterectomy rates between groups because we have
already shown that hysterectomy is unrelated to can-
cer mortality in this cohort.15 We were unable to
adjust our results for other lifestyle or familial vari-
ables. Residual confounding therefore could be an
alternative explanation for our findings.

The study has been prone to large losses to follow-
up. Thus our main dataset contained only 67% of the
potential 1.656,000 woman years of observation
which would have occurred if no one had been lost
to follow-up. Biased results could have occurred if
there was a relation between leaving the study, con-
traceptive pill use, and cancer risk. We have pre-
viously shown that women lost to general princi-
pal follow-up had similar mortality risks as
those still under observation,16 suggesting no major
systematic bias from loss to follow-up. In case our
main dataset results were affected by the censoring
of flagged never users younger than 38 when lost to
general practitioner follow-up before 1996, we car-
ried out an analysis in which both flagged ever users
and never users satisfying these criteria were
excluded. The adjusted relative risk for any cancer
was 0.95 (95% confidence interval 0.88 to 1.02).

Our wish to maximise the amount of data available
for analysis and to use cancer information supplied
by the Office for National Statistics for flagged
women introduced a degree of uncertainty into the
interpretation of our findings. The main dataset ana-
lyses may have been prone to misclassification of
exposure status as we assumed that never users
older than 38 years who left the study did not sub-
sequently start oral contraception. The level of
misclassification is likely to have been small and its
effect will have been to underestimate pill related
cancer risks. Depending on which dataset was ex-
amined, our results suggest either a 12% or 3% reduction
in overall cancer risk from oral contraception. It is
worth noting, however, that these overall risks are
average effects among pill users. The analyses about
duration of use showed that long term (>8 year) users
had an increased risk of any cancer (adjusted relative
risk 1.22, 95% confidence interval 1.07 to 1.39). It is
important to remember, however, that comparati-
vely few women in our study used oral contracep-
tives for such durations, with less than a quarter of
users being at this increased risk.

Overall mortality in the cohort was about 20% lower
than the national average in 1999,7 mainly because
women with chronic disease were not recruited to the
study.11 Although this may have affected the generali-
sability of the results it tends to affect estimates of abso-
lute rather than relative risk.

Most of the pills used in the study were combined oral
contraceptives containing 50 µg of oestrogen (75%;
>50 µg, 12%; <50 µg, 10%; progestogen only prepara-
tions, 8%). Most women used preparations from more
than one oestrogen dose category, almost entirely in a
downwards direction—that is, from a >50 µg to a 50 µg
preparation, or from a 50 µg to <30 µg preparation. This
pattern of usage meant that it would be impossible to
determine whether any associations between cancer
and oestrogen dosage group were due to the effects of
preparations used most recently before the cancer diag-
nosis, or were lingering effects from previous use of a
higher dose formulation. We could not, therefore, ex-
amine cancer risk by hormonal content of pills used. Nota-
ibly, only 566 women exclusively used products
containing <50 µg oestrogen.

Table 4 | Risk of cancer by duration of oral contraceptive use in general practitioner observation dataset

<table>
<thead>
<tr>
<th>Malignancies</th>
<th>ICD-8</th>
<th>Oral contraceptive use &lt;48 months</th>
<th></th>
<th>Oral contraceptive use 49-96 months</th>
<th></th>
<th>Oral contraceptive use ≥97 months</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Rate* (No of women)</td>
<td>Relative risk† (95% CI)</td>
<td>Rate* (No of women)</td>
<td>Relative risk† (95% CI)</td>
<td>Rate* (No of women)</td>
<td>Relative risk† (95% CI)</td>
</tr>
<tr>
<td>Large bowel or rectum</td>
<td>153-154</td>
<td>21.47 (24)</td>
<td>0.82 (0.51 to 1.31)</td>
<td>19.04 (19)</td>
<td>0.72 (0.43 to 1.21)</td>
<td>25.01 (23)</td>
<td>0.95 (0.59 to 1.54)</td>
</tr>
<tr>
<td>Gallbladder or liver</td>
<td>155-156</td>
<td>3.45 (3)</td>
<td>1.23 (0.31 to 4.93)</td>
<td>1.18 (1)</td>
<td>0.42 (0.05 to 3.51)</td>
<td>4.25 (3)</td>
<td>1.52 (0.38 to 6.07)</td>
</tr>
<tr>
<td>Lung</td>
<td>162</td>
<td>21.03 (24)</td>
<td>1.12 (0.67 to 1.87)</td>
<td>13.89 (15)</td>
<td>0.74 (0.41 to 1.35)</td>
<td>25.26 (23)</td>
<td>1.35 (0.83 to 2.19)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>172</td>
<td>14.13 (20)</td>
<td>0.95 (0.54 to 1.64)</td>
<td>11.84 (12)</td>
<td>0.79 (0.41 to 1.53)</td>
<td>25.56 (17)</td>
<td>1.71 (0.96 to 3.06)</td>
</tr>
<tr>
<td>Breast</td>
<td>174</td>
<td>105.24 (131)</td>
<td>1.00 (0.81 to 1.23)</td>
<td>100.19 (92)</td>
<td>0.95 (0.75 to 1.21)</td>
<td>128.23 (144)</td>
<td>1.22 (0.97 to 1.52)</td>
</tr>
<tr>
<td>Invasive cervix</td>
<td>180</td>
<td>15.43 (23)</td>
<td>1.10 (0.64 to 1.90)</td>
<td>20.26 (23)</td>
<td>1.45 (0.84 to 2.49)</td>
<td>38.12 (26)</td>
<td>2.73 (1.61 to 4.61)</td>
</tr>
<tr>
<td>Uterine body</td>
<td>182</td>
<td>8.08 (10)</td>
<td>0.60 (0.30 to 1.21)</td>
<td>1.87 (2)</td>
<td>0.14 (0.03 to 0.58)</td>
<td>7.69 (9)</td>
<td>0.57 (0.27 to 1.19)</td>
</tr>
<tr>
<td>Ovary</td>
<td>183</td>
<td>11.90 (15)</td>
<td>0.58 (0.33 to 1.04)</td>
<td>11.63 (12)</td>
<td>0.57 (0.30 to 1.07)</td>
<td>7.69 (6)</td>
<td>0.38 (0.16 to 0.88)</td>
</tr>
<tr>
<td>Central nervous system or pituitary</td>
<td>191, 1943</td>
<td>2.16 (5)</td>
<td>1.70 (0.34 to 8.42)</td>
<td>4.73 (5)</td>
<td>3.73 (0.89 to 15.59)</td>
<td>7.00 (6)</td>
<td>5.51 (1.38 to 22.05)</td>
</tr>
<tr>
<td>Site unknown</td>
<td>199</td>
<td>6.54 (8)</td>
<td>0.71 (0.32 to 1.59)</td>
<td>2.86 (3)</td>
<td>0.31 (0.09 to 1.04)</td>
<td>10.57 (11)</td>
<td>1.16 (0.57 to 2.36)</td>
</tr>
<tr>
<td>Other cancers</td>
<td>92.84 (119)</td>
<td>0.93 (0.75 to 1.16)</td>
<td>85.07 (83)</td>
<td>0.85 (0.66 to 1.10)</td>
<td>113.92 (103)</td>
<td>1.14 (0.91 to 1.44)</td>
<td></td>
</tr>
<tr>
<td>Main gynaecological</td>
<td>180,182,183</td>
<td>35.45 (48)</td>
<td>0.74 (0.53 to 1.03)</td>
<td>33.80 (37)</td>
<td>0.70 (0.49 to 1.02)</td>
<td>53.43 (41)</td>
<td>1.11 (0.78-1.59)</td>
</tr>
<tr>
<td>Any cancer</td>
<td>140-209</td>
<td>286.77 (359)</td>
<td>0.93 (0.82-1.06)</td>
<td>262.13 (253)</td>
<td>0.87 (0.74-0.98)</td>
<td>375.18 (324)</td>
<td>1.22 (1.07-1.39)</td>
</tr>
</tbody>
</table>

ICD-8=international classification of diseases, eighth revision. Tests for trend were all non-significant (P>0.05), except for invasive cancer of cervix (P=0.001) and cancer of uterine body (P=0.0287), ovary (P=0.0015), and central nervous system or pituitary (P=0.0112).

*Standardised rate per 100 000 woman years, adjusted for age, parity, smoking, social status, and ever use of hormone replacement therapy.

†Never users as baseline.
The pattern of cancer risk seen in this study is consistent with that observed in many other studies. The reduced risk of main gynaecological cancers among ever users of oral contraceptives was almost identical to that observed by the Oxford/Family Planning Association contraceptive study and contrasts with an earlier report from our study. In the earlier publication, a large proportion of the ever user experience related to current rather than past oral contraceptive use, and many women were just entering the age when the incidence of uterine body and ovarian cancer rises. In this paper much more of the data on oral contraception related to past use, and the cohort was older. We are unable to explain the increased risks among ever users for cancer of the central nervous system or pituitary. None of these cancers were notified as being of pituitary origin, although the frequent lack of a post mortem may have resulted in some misclassification of central nervous system events.

Many women, especially those who used the first generation of oral contraceptives many years ago, are likely to be reassured by our results. Our findings might not, however, reflect the experience of women using oral contraceptives today, if currently available preparations have a different risk to earlier products, or if differences in patterns of usage (such as age at starting oral contraceptives or duration of use) materially affect cancer risk. Although relatively limited, current evidence suggests that lower oestrogen dose formulations provide similar protection from uterine body and ovarian cancer as older, higher dose preparations.

The reanalysis of original data on breast cancer also found little difference in risk between preparations.

Public health implications

In our study oral contraception was not associated with a significantly increased risk of any cancer. Indeed in the main dataset the estimated overall absolute reduction in risk of any cancer among ever users of combined oral contraceptives was 45 per 100 000 woman years, with greater benefits in older rather than younger women (age 30-39: 34 per 100 000; 40-49: 24 per 100 000; 50-59: 90 per 100 000; ≥60: 47 per 100 000). In the smaller general practitioner observation dataset the estimated absolute risk reduction was 10 per 100 000 woman years. These results suggest that, at least in this relatively healthy UK cohort, the cancer benefits associated with oral contraception outweigh the risks.

The level of cancer reduction seen in different parts of the world will depend on factors such as levels of oral contraception usage, duration of use, age at stopping, and the incidence of different cancers. Further work is needed therefore to quantify the likely balance of cancer risks and benefits in different parts of the world, including effects on mortality.

Table 5 | Risk of cancer by time since last oral contraceptive use in general practitioner observation dataset

<table>
<thead>
<tr>
<th>Malignancies</th>
<th>Current and r60</th>
<th>61-120</th>
<th>121-180</th>
<th>181-240</th>
<th>≥241</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rate* (No of women)</td>
<td>Relative risk† (95% CI)</td>
<td>Rate* (No of women)</td>
<td>Relative risk† (95% CI)</td>
<td>Rate* (No of women)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large bowel or rectum</td>
<td>12.94 (12)</td>
<td>0.49 (0.26 to 0.92)</td>
<td>26.75 (15)</td>
<td>1.02 (0.58 to 1.79)</td>
<td>34.19 (15)</td>
</tr>
<tr>
<td>Gallbladder or liver</td>
<td>3.03 (1)</td>
<td>1.08 (0.13 to 8.98)</td>
<td>2.08 (1)</td>
<td>0.74 (0.09 to 6.18)</td>
<td>4.15 (2)</td>
</tr>
<tr>
<td>Lung</td>
<td>15.09 (11)</td>
<td>0.81 (0.41 to 1.57)</td>
<td>15.28 (13)</td>
<td>0.82 (0.44 to 1.53)</td>
<td>13.84 (13)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>17.46 (20)</td>
<td>1.17 (0.67 to 2.03)</td>
<td>23.46 (12)</td>
<td>1.57 (0.81 to 3.03)</td>
<td>7.62 (5)</td>
</tr>
<tr>
<td>Breast</td>
<td>87.50 (116)</td>
<td>0.83 (0.67 to 1.03)</td>
<td>110.76 (69)</td>
<td>1.05 (0.80 to 1.37)</td>
<td>134.13 (82)</td>
</tr>
<tr>
<td>Invasive cervix</td>
<td>27.89 (47)</td>
<td>1.99 (1.26 to 3.15)</td>
<td>17.41 (13)</td>
<td>1.25 (0.65 to 2.39)</td>
<td>35.41 (7)</td>
</tr>
<tr>
<td>Uterine body</td>
<td>3.23 (5)</td>
<td>0.24 (0.09 to 0.61)</td>
<td>2.43 (1)</td>
<td>0.18 (0.02 to 1.32)</td>
<td>7.61 (6)</td>
</tr>
<tr>
<td>Ovary</td>
<td>10.16 (9)</td>
<td>0.50 (0.24 to 1.01)</td>
<td>8.51 (6)</td>
<td>0.62 (0.18 to 0.97)</td>
<td>5.77 (5)</td>
</tr>
<tr>
<td>Central nervous system of pituitary</td>
<td>8.21 (5)</td>
<td>6.47 (1.55 to 27.07)</td>
<td>2.26 (2)</td>
<td>1.78 (0.30 to 10.64)</td>
<td>2.31 (2)</td>
</tr>
<tr>
<td>Site unknown</td>
<td>3.34 (4)</td>
<td>0.36 (0.13 to 1.05)</td>
<td>6.42 (4)</td>
<td>0.70 (0.24 to 2.02)</td>
<td>9.22 (8)</td>
</tr>
<tr>
<td>Other cancers</td>
<td>57.80 (80)</td>
<td>0.58 (0.45 to 0.75)</td>
<td>102.99 (58)</td>
<td>1.03 (0.77 to 1.38)</td>
<td>77.11 (63)</td>
</tr>
<tr>
<td>Main gynaecological</td>
<td>41.36 (61)</td>
<td>0.86 (0.63 to 1.18)</td>
<td>28.39 (20)</td>
<td>0.59 (0.37 to 0.95)</td>
<td>48.87 (18)</td>
</tr>
<tr>
<td>Any cancer</td>
<td>239.75 (303)</td>
<td>0.78 (0.68 to 0.89)</td>
<td>305.04 (183)</td>
<td>0.99 (0.84 to 1.16)</td>
<td>313.62 (191)</td>
</tr>
</tbody>
</table>

Tests for trend were all non-significant (P>0.05), except for main gynaecological cancers (P=0.041).

†Standardised rate per 100 000 woman years, adjusted for age, parity, smoking, social status, and ever use of hormone replacement therapy.
Oral contraception may produce a net benefit, with absolute risk reduction estimated at 10 or
Oral contraception is not associated with an overall increased risk of cancer
WHAT THIS STUDY ADDS
unknown
The absolute overall balance of incident cancer associated with oral contraception is
risk of others
Oral contraceptives are associated with an increased risk of some cancers and a decreased
WHAT IS ALREADY KNOWN ON THIS TOPIC
Oral contraceptives are associated with an increased risk of some cancers and a decreased
risk of others
The absolute overall balance of incident cancer associated with oral contraception is unknown

We thank Clifford Kay, who established and ran the study for its first 26 years, the general practitioners who contributed data, and Aileen Murphy for administrative support of the database. AIME is supported by a Wellcome Trust research career development fellowship.

Contributors: PCH had the original idea, advised on and checked the analysis, and wrote the first and subsequent drafts of the paper. He is guarantor of the paper. SS was responsible for data analysis; under the supervision of AL. AIME was responsible for regularly updating the database with cancer information. AME, with AL, checked the validity of the programme used to analyse the data, and, with LI, checked the data extractions and analyses. VA maintains the main study database and extracted data for analysis. All authors contributed to the scientific development of the paper, commented on successive drafts, and agreed to the final manuscript.

Funding: This study received funding from the Royal College of General Practitioners, Medical Research Council, Imperial Cancer Research Fund, British Heart Foundation, Schering AG, Schering Health Care, Wyeth Ayerst International, Ortho Cilag, and Searle.

Competing interests: None declared.

Ethical approval: The study was established before the introduction of research ethics committees in the United Kingdom. Even so, procedures were used to maintain the confidentiality of women. Correspondence between the general practitioners who contributed data, and the study, used a unique study number; the key to which only the general practitioners knew.


Accepted: 9 July 2007
Preventive strategies for group B streptococcal and other bacterial infections in early infancy: cost effectiveness and value of information analyses

Tim E Colbourn, research fellow,1 Christian Asseburg, research fellow,2 Laura Bojke, research fellow,2 Zoe Philips, lecturer,3 Nicky J Welton, senior research fellow in medical statistics,4 Karl Claxton, professor,2 A E Ades, professor,4 Ruth E Gilbert, professor1

ABSTRACT

Objective To determine the cost effectiveness of strategies for preventing neonatal infection with group B streptococci and other bacteria in the UK and the value of further information from research.

Design Use of a decision model to compare the cost effectiveness of prenatal testing for group B streptococcal infection (by polymerase chain reaction or culture), prepartum antibiotic treatment (intravenous penicillin or oral erythromycin), and vaccination during pregnancy (not yet available) for serious bacterial infection in early infancy across 12 maternal risk groups. Model parameters were estimated using multi-parameter evidence synthesis to incorporate all relevant data inputs.

Data sources 32 systematic reviews were conducted: 14 integrated results from published studies, 24 involved analyses of primary datasets, and five included expert opinion.

Main outcomes measures Healthcare costs per quality adjusted life year (QALY) gained.

Results Current best practice (to treat only high risk women without prior testing for infection) and universal testing by culture or polymerase chain reaction were not cost effective options. Immediate extension of current best practice to treat all women with preterm and high risk term deliveries is readily achievable and would be beneficial. The choice between adding culture testing for low risk women or vaccination for all should be informed by further research. Trials to evaluate vaccine efficacy should be prioritised.

INTRODUCTION

Screening to prevent early onset, group B streptococcal infection in neonates has been established in the United States for the past decade and results in about 30-50% of women receiving intravenous prophylactic antibiotics during labour.1-2 Although most other Western countries offer culture-based testing for maternal colonisation with group B streptococci or risk-based testing and treatment, screening is not currently recommended in the United Kingdom because of lack of evidence of effectiveness.3-5

The controversy centres on three factors. Firstly, is the incidence of early onset neonatal infection high enough in the UK for the benefits to outweigh the costs? Secondly, would the benefits of routine testing be worth while over and above existing use of prepartum antibiotics as part of good clinical practice (such as for maternal fever or preterm rupture of the membranes before the onset of labour)?6-8 Thirdly, would it be better to await the development of a vaccine for group B streptococcal infection in pregnant women?9-11 This could be available within the next 5-10 years and would be expected to have an impact on both early and late onset infection in early infancy (personal communications, CJ Baker, Baylor College of Medicine, USA, and P Heath, St George’s, University of London).

We report the first cost effectiveness analysis to consider the impact of testing for maternal group B streptococcal colonisation, prepartum antibiotic treatment, and vaccination on all types of early onset serious bacterial infection. In this report, we focus on the cost effectiveness of options that can be decided on now, when vaccination is not yet available. In the value of information analyses, we address future options, including vaccination, and assess how much it would be worth investing to obtain further information before making a decision.

METHODS

Population, interventions, and outcomes

We constructed a decision model to quantify the effects of different prenatal testing, treatment, and vaccination strategies on serious bacterial infection in early
The pathway of events is shown in fig 1. We separately analysed the intervention strategies for each of 12 maternal risk groups, representing testing and treatment options faced by clinicians assessing a woman presenting in suspected labour (fig 1). We assumed that antibiotic prophylaxis was started when a woman presents in labour or with preterm rupture of membranes. The interventions considered were doing nothing; testing vaginal and rectal swabs by culture at 35–37 weeks’ pregnancy and treating women with at least one positive result with either oral erythromycin or intravenous penicillin; testing swabs by polymerase chain reaction (PCR) at presentation in labour and treating those with a positive result with oral erythromycin or intravenous penicillin; oral or intravenous treatment without testing; and vaccination at 28 weeks, either given alone or in addition to each of the six other active interventions.

Early and late onset infections were defined by positive culture from blood or cerebrospinal fluid. Outcomes were measured in quality adjusted life years (QALYs) gained for births at or after 24 weeks of gestation for the lifetime of the child.

### Table 1 Parameter estimates for the risks of bacterial infection in untreated preterm and term deliveries. Values are means (95% confidence intervals) unless stated otherwise

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preterm deliveries</th>
<th>Term deliveries</th>
<th>Overall mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of transmission of GBS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal colonisation (%)</td>
<td>23.8 (17.2 to 31.4)</td>
<td>11.1 (8.3 to 14.8)</td>
<td>12.2 (9.0 to 15.9)</td>
</tr>
<tr>
<td>Baby colonisation given maternal colonisation (%)</td>
<td>36.6 (28.4 to 45.9)</td>
<td>31.5 (24.1 to 40.0)</td>
<td>32.4 (24.7 to 40.8)</td>
</tr>
<tr>
<td>Early onset GBS given baby colonisation (%)</td>
<td>2.2 (1.5 to 3.2)</td>
<td>1.1 (0.7 to 1.6)</td>
<td>1.3 (0.9 to 1.8)</td>
</tr>
<tr>
<td>Risk of infection in baby per 1000 live births</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early onset GBS</td>
<td>1.84 (1.53 to 2.19)</td>
<td>0.38 (0.33 to 0.42)</td>
<td>0.48 (0.44 to 0.53)</td>
</tr>
<tr>
<td>Early onset infection other than GBS</td>
<td>6.97 (5.19 to 9.01)</td>
<td>0.50 (0.36 to 0.65)</td>
<td>0.97 (0.81 to 1.14)</td>
</tr>
<tr>
<td>Late onset GBS</td>
<td>1.51 (1.20 to 1.84)</td>
<td>0.15 (0.11 to 0.17)</td>
<td>0.25 (0.21 to 0.28)</td>
</tr>
</tbody>
</table>

### Table 2 Estimated relative risks and costs associated with treatments for neonatal group B streptococcal infection. Values are means (95% confidence intervals) unless stated otherwise

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Intravenous penicillin</th>
<th>Oral penicillin or erythromycin</th>
<th>Vaccination (expert opinion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal colonisation</td>
<td>NA</td>
<td>NA</td>
<td>0.66 (0.44 to 0.85)</td>
</tr>
<tr>
<td>Early onset GBS stillbirth</td>
<td>0.69 (0.23 to 0.97)</td>
<td>NA</td>
<td>0.38 (0.11 to 0.73)</td>
</tr>
<tr>
<td>Early onset GBS live birth*</td>
<td>0.03 (0.00 to 0.12)</td>
<td>0.28 (0.02 to 0.61)</td>
<td>0.38 (0.11 to 0.73)</td>
</tr>
<tr>
<td>Early onset infection other than GBS</td>
<td>0.73 (0.64 to 0.81)</td>
<td>0.74 (0.44 to 1.21)</td>
<td>NA</td>
</tr>
<tr>
<td>Late onset GBS</td>
<td>NA</td>
<td>NA</td>
<td>0.20 (0.06 to 0.42)</td>
</tr>
</tbody>
</table>

**GBS**=group B streptococcal infection. NA=not assessed.

*Effect given maternal colonisation.

Data sources and evidence synthesis

We conducted systematic reviews to answer 32 questions to inform model parameters. We used published studies to answer 14 questions, primary datasets for 24 questions, and expert opinion for five questions. One question (vaccine efficacy) relied solely on expert opinion. Details of each review and data sources are given in the full report.

We used multi-parameter evidence synthesis to simultaneously estimate each model parameter using all relevant data inputs that directly or indirectly informed the parameters. The model parameters for infection outcomes and treatment effectiveness are summarised in tables 1 and 2. Further details are in the full report.

Cost effectiveness analysis, decision uncertainty, and value of information analyses

The perspective of the cost effectiveness analysis was the NHS. We calculated the expected costs and QALYs (relative to doing nothing) for each active intervention within each risk group using a threshold of £25000 per QALY gained.

Although antibiotic treatment for all women was the most cost effective option, we judged that universal treatment would be unacceptable because of concerns about antibiotic resistance and the medicalisation of labour. We therefore restricted antibiotic use by stipulating that women delivering at term with no risk factors (group 12) could not be treated without a positive test result. We also applied this criterion to term deliveries with prolonged rupture of membranes (group 11) as these two groups are indistinguishable at presentation in suspected labour.

We conducted analyses for each of the 12 risk groups and then for all possible combinations of interventions that had more than a 1% probability of being cost effective in each risk group. We made an exception to the 1% rule to include three intervention strategies relevant to UK healthcare policy for comparison—the recommendations of the Royal College of Obstetricians and Gynaecologists, the college’s recommendations plus oral treatment for preterm ruptured membranes before onset of labour (risk group 5) (which we termed “current best practice”), and the experimental intervention arm of a proposed cluster randomised trial of 540000 UK women for the Health Technology Assessment (HTA) Programme expected to cost about £12m (Brocklehurst et al, Antenatal screening for group B streptococcus colonisation—protocol development, available at www.hta.nhsweb.nhs.uk/).

We quantified the potential value of further research by calculating the “expected value of perfect information” for the UK population based on the difference between the expected net benefit with perfect information and that with current information and assuming a 10 year time horizon.
RESULTS

Model parameters

The prevalence of maternal colonisation was twice as high in preterm deliveries compared with term deliveries (table 1). The overall incidence of early onset neonatal group B streptococcal infection was 0.48/1000 live births but was highest risk in preterm deliveries by women with a previous positive vaginal swab or urine culture for group B streptococci (risk group 3), fever (group 4), or preterm rupture of the membranes before onset of labour (group 5) (see full report6). Among term deliveries, the corresponding risk groups (9, 10, and 11) also had the highest risk. Table 2 shows the treatment effects estimated by the model. Culture testing at 35-37 weeks' pregnancy had lower sensitivity and specificity (75.8% (95% confidence interval 47.2% to 91.5%) and 94.7% (88.5% to 98.5%)) than PCR testing (89.2% (49.1% to 98.7%) and 95.8% (86.7% to 99.7%)) but was cheaper (£11.99 per woman v £19.03 per woman).

Cost effectiveness results

Testing for maternal colonisation with group B streptococci was not cost effective for the 20% of women in risk groups 1 to 10 (table 3). In these groups, maternal testing, whether by culture or PCR, had a probability of ≤1% of being cost effective. Because of the insensitivity of culture testing and the predominance of infection with pathogens other than group B streptococci (table 1), women delivering preterm infants were always better off being treated without testing. However, there is uncertainty about whether the greater expense of intravenous treatment is outweighed by its greater effectiveness compared with oral treatment. The economic importance of this uncertainty is reflected in the high expected value of information for risk groups 1, 5, and 6 (table 3). Among term deliveries, the value of information was highest for groups 11 and 12, who could not be treated without a positive test result. For the 71% of women with no risk factors, culture testing was most likely to be cost effective, but PCR testing and doing nothing could not be ruled out as potentially cost effective strategies (table 3).

The large number of potential combinations of interventions for the 12 maternal risk groups were reduced to 341 strategies, without vaccination, based on pragmatic considerations (detailed in the full report6). Figure 2 shows the expected costs and QALYs for each strategy compared with doing nothing. Points to the bottom and right are less costly, provide more QALYs, and have a higher net benefit. The dotted net benefit isoline represents the maximum available net benefit. Separate “clouds” of strategies can be distinguished for treating without testing (lowest cloud), culture testing, and PCR testing (most expensive of the three). Within each cloud, QALYs are gained (moving to the right) by strategies that maximise the proportion of women treated without testing.

Table 4 lists the results for strategies on the cost effectiveness frontier (the solid line joining strategies with least increase in costs per QALY gained). All involve treatment without testing for all risk groups except 11 and 12, and the strategy with the maximum net benefit involves culture testing for the low risk, term women (groups 11 and 12). On average, this is the most cost effective option, but several other strategies, with minor changes in treatment for specific risk groups, yield similar net benefit. Replacement of culture testing with PCR testing is only marginally less cost effective because PCR was more sensitive but also more expensive than culture. Current best practice, the recommendations of the Royal College of Obstetricians and Gynaecologists, and the experimental intervention arm of the proposed HTA trial generate substantially less net benefit and are clearly not cost effective (fig 2 and table 4).
Minimisation of antibiotic use

Two limitations of our analyses are the exclusion of adverse effects of antibiotics and organisational costs to implement (or reverse) a new intervention. To address these limitations, we propose a series of policy options in table 4, assuming that there is concern about antibiotic exposure and that adding to rather than changing current practice would be easier to implement.

We start with current best practice in the UK, which is clearly superior to the recommendations of the Royal College of Obstetricians and Gynaecologist and involves treating 7.4% of women with antibiotics, with a net benefit for the UK per year of £21.4m compared with doing nothing (table 4). Extending the clinical recommendations for treating without testing to include all women delivering preterm (and continuing to treat high risk term women) would increase net benefit to £46.5m but would nearly double the proportion of women treated (21%). Further extending treatment without testing to risk groups 1-10 with culture testing for groups 11 and 12 generates slightly more net benefit (£48.5m) but is unlikely to be acceptable as the proportion of women treated would rise to 27%. If policy makers were to limit options to those based on treating only high risk groups without testing or the experimental intervention arm of the proposed HTA trial (top 4 strategies in table 4), pending further research on culture or PCR testing, the probability of being cost effective would be 0.92 for treating all preterm and high risk term women, 0.03 for current best practice, 0.00 for the royal college’s recommendations, and 0.05 for the proposed trial intervention.

Value of information analyses

Assuming that vaccination is not available, the expected value of perfect information for the UK for choosing between all the strategies is £28.9m. As table 3 shows, most of the value of information is

<table>
<thead>
<tr>
<th>Maternal risk groups in hierarchical order</th>
<th>% of total population</th>
<th>Intervention</th>
<th>Probability of being cost effective</th>
<th>Expected value of information per year in UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm deliveries (&lt;37 weeks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Planned caesarean section</td>
<td>0.80</td>
<td>IV antibiotic</td>
<td>0.5870</td>
<td>£5 281 333</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.4120</td>
<td></td>
</tr>
<tr>
<td>2. Previous baby with GBS</td>
<td>0.01</td>
<td>IV antibiotic</td>
<td>0.8590</td>
<td>£7 820</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.1370</td>
<td></td>
</tr>
<tr>
<td>3. Positive urine or vaginal swab for GBS in current pregnancy</td>
<td>0.44</td>
<td>IV antibiotic</td>
<td>0.9730</td>
<td>£81 600</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.0178</td>
<td></td>
</tr>
<tr>
<td>4. Fever ≥38.0°C in labour</td>
<td>0.25</td>
<td>IV antibiotic</td>
<td>0.7800</td>
<td>£539 467</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.2160</td>
<td></td>
</tr>
<tr>
<td>5. Rupture of membranes before onset of labour</td>
<td>2.41</td>
<td>IV antibiotic</td>
<td>0.5800</td>
<td>£12 806 667</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.4190</td>
<td></td>
</tr>
<tr>
<td>6. Spontaneous labour (membrane rupture ≤2 hours before or after onset of labour)</td>
<td>3.43</td>
<td>IV antibiotic</td>
<td>0.8590</td>
<td>£4 193 333</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.1370</td>
<td></td>
</tr>
<tr>
<td>Term deliveries (≥37 weeks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Planned caesarean section</td>
<td>7.99</td>
<td>Oral antibiotic</td>
<td>0.6720</td>
<td>£1 586 667</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IV antibiotic</td>
<td>0.3270</td>
<td></td>
</tr>
<tr>
<td>8. Previous baby with GBS</td>
<td>0.08</td>
<td>IV antibiotic</td>
<td>0.6060</td>
<td>£30 600</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.3930</td>
<td></td>
</tr>
<tr>
<td>9. Positive urine or vaginal swab for GBS in current pregnancy</td>
<td>3.51</td>
<td>IV antibiotic</td>
<td>0.9730</td>
<td>£68 000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.0242</td>
<td></td>
</tr>
<tr>
<td>10. Fever ≥38.0°C in labour</td>
<td>1.60</td>
<td>IV antibiotic</td>
<td>0.7170</td>
<td>£581 400</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral antibiotic</td>
<td>0.2720</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCR testing, IV antibiotic</td>
<td>0.0102</td>
<td>£4 533 333</td>
</tr>
<tr>
<td>11. Membrane rupture for ≥18 hours</td>
<td>8.37</td>
<td>PCR testing, IV antibiotic</td>
<td>0.5760</td>
<td>£2 040 000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Culture testing, IV antibiotic</td>
<td>0.2000</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCR testing, oral antibiotic</td>
<td>0.1820</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Culture testing, oral antibiotic</td>
<td>0.0418</td>
<td></td>
</tr>
<tr>
<td>12. No risk factors</td>
<td>71.10</td>
<td>Culture testing, IV antibiotic</td>
<td>0.8390</td>
<td>£2 040 000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCR testing, IV antibiotic</td>
<td>0.0952</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nothing</td>
<td>0.0640</td>
<td></td>
</tr>
</tbody>
</table>

*Culture testing not listed for risk groups 1-10 because of zero probability of being cost effective. GBS = group B streptococcal infection. IV = intravenous. PCR = polymerase chain reaction.
Driven by uncertainty about the choice between intravenous and oral antibiotic treatment for certain preterm groups.

However, if decisions are to be postponed pending further information from research, the future availability of vaccination needs to be considered. Cost effectiveness analyses, reported in detail in the full report,\(^a\) show that the gain in net benefit from vaccination, when added to the best non-vaccination strategy (treat without testing for groups 1-10 and culture based testing for groups 11 and 12) is small (£2.1m/year in the UK) and uncertain. Strategies involving testing for low-risk women in addition to vaccination prevent more cases of infection but, because of the added cost of testing, produce less net benefit. Vaccination is therefore more cost effective without testing.

If vaccination is included as an option the expected value of information is more than doubled (£67.3m), reflecting the potential but uncertain increased net benefit and increased options. These estimates are moderately large and, although they provide only an upper bound on the value of a new study, clearly exceed the cost of most proposed research in this area. Further research may well be worth while provided it addresses the uncertainties highlighted by these analyses.

**DISCUSSION**

Our results show that current best practice in the UK is clearly not cost effective. All cost effective options involve treating all preterm and high-risk term groups without testing. Testing high-risk women for group B streptococcal colonisation would not be cost effective, as even those with negative results would be better off treated to reduce the risk of early onset infection due to pathogens other than group B streptococcus. Culture testing of low-risk term women, combined with treatment without testing for the rest, would be the most cost effective strategy.

In deciding future policy, the value of information analyses suggest that moderate investment in research could be worth while provided studies address the uncertainties highlighted by our analyses. Vaccination plus treatment of all preterm and high-risk term women offers a more cost effective strategy with less antibiotic exposure than one involving culture testing of low-risk women, but the difference in net benefit is uncertain and based on expert opinion on vaccine efficacy.

**Strengths and limitations of study**

The strengths of our study include analysis of 12 maternal risk groups to reflect the decision options faced by clinicians and inclusion of all available data that directly and indirectly informed parameters. One limitation is the restriction of outcomes to the current pregnancy, which underestimates net benefits of vaccination for subsequent births.\(^5\) Another is that we focused on culture-positive bacteraemia or meningitis. Had we included culture-negative sepsis, the net benefit would have been higher but the ranking of strategies would not have changed. A third limitation was that we did not include adverse effects of intrapartum antibiotic treatment on pathogen selection and antibiotic resistance in the net costs or QALYs. As a result, we underestimated the benefits of strategies that involved treating fewer women. We quantified the trade-off that policy makers would need to make in terms of additional women treated per QALY gained (see section 7 of the full report\(^8\)).

**Policy issues**

We suggest that policy makers consider immediate extension of current practice to give antibiotic treatment to all women with preterm and high-risk term deliveries. The organisational costs of moving from current practice to treating all high-risk women (risk groups 1-6, 8-10) would be minimal, and all the more cost effective strategies in our study require treatment of these high-risk groups. Our study showed that these groups should be treated, as the probability of doing nothing being cost effective was less than 0.01 in each risk group, but there was uncertainty about whether antibiotic treatment should be oral or intravenous, especially for women with preterm membrane rupture before onset of labour. Currently, these women receive oral treatment at presentation with membrane rupture. This could be changed to intravenous treatment during labour—rather than stopping treatment altogether, as currently happens.

Assuming treatment of all preterm and high-risk term women is adopted, the most cost effective option would be to add culture testing for low-risk women (risk groups 7, 11, and 12). This option is unlikely to be adopted without further research.

Firstly, the UK National Screening Committee requires evidence from high-quality randomised controlled trials that the screening programme is effective.

---

**Fig 2** Cost effectiveness of strategies (excluding vaccination). The dotted line denotes maximum net benefit. The solid line denotes the cost effectiveness frontier. (HTA=Health Technology Assessment, PCR=Polymerase chain reaction, RCOG=Royal College of Obstetricians and Gynaecologists.)
in reducing mortality or morbidity. Syntheses of studies of treatment efficacy and of test accuracy may not be regarded as sufficient. The claim that high quality trials are lacking is the principal rationale for the proposed £12m HTA trial of culture screening compared with current best practice.

Secondly, providing culture testing for low risk pregnancies will involve start-up costs (staff training, set up of laboratories, and quality control) that could be substantial and would not be recouped if a vaccination strategy without culture testing is subsequently adopted. Given that further research is likely to be a prerequisite for implementation of culture testing, the cost effectiveness of such research should be considered alongside other information needed to inform future preventive options, including vaccination.

Our value of information analyses suggest that moderate investment in research could be worth while provided studies address the uncertainties highlighted by our analyses. Further investigation of the type of research required to reduce the uncertainties in cost effectiveness analyses is possible by carrying out expected value of sample information calculations, but these are technically challenging and beyond the scope of this report. The value of information was highest when vaccination was included as an option, and our analyses for each maternal risk group suggest that the main uncertainty relates to vaccine efficacy, which was based solely on expert opinion (see full report).

Trials of vaccine efficacy and safety would also be a prerequisite for licensing of the candidate vaccines currently being pursued by industry. For example, a group B streptococcal glycoconjugate vaccine may be available for use before conception or during adolescence within the next five years (personal communications, C J Baker, Baylor College of Medicine, USA). Such efficacy trials are likely to use surrogate outcomes based on serological markers of a protective immune response, since trials to assess neonatal infection would need to be extremely large. Extensive post-marketing surveillance for effectiveness and safety would be an integral part of a licensing strategy (personal communications, C J Baker, Baylor College of Medicine, USA, and P Heath, St George’s, University of London). Vaccination during pregnancy requires careful consideration of safety, but several inactivated vaccines are currently recommended, particularly during the second and third trimesters (www.cdc.gov/vaccines/pubs/downloads/f_preg_chart.pdf).

If policy makers judge that vaccination is not an option, the amount worth investing in further information would be halved (to £29m), and priorities for further information would be the effectiveness of intravenous versus oral antibiotic treatment in some preterm risk groups on all types of early onset neonatal infection.

Table 4 | Cost effectiveness (relative to no intervention) in order of QALYs gained of strategies relevant to policy or on the “cost effectiveness frontier” (see fig 2 for explanation)

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Intervention for each maternal risk group</th>
<th>Cost (£m)</th>
<th>QALYs gained</th>
<th>Expected net benefit (£m)*</th>
<th>Antibiotic exposure (% of population)</th>
<th>% of infections prevented (%)†</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCOG guidelines</td>
<td>N I I I O N N I I I N N</td>
<td>-1.2</td>
<td>340</td>
<td>9.7</td>
<td>5.2</td>
<td>5.3</td>
<td>Control arm for proposed HTA trial</td>
</tr>
<tr>
<td>Current best practice</td>
<td>N I I I O N N I I I N N</td>
<td>-2.9</td>
<td>741</td>
<td>21.4</td>
<td>7.4</td>
<td>10.1</td>
<td>Intervention arm for proposed HTA trial</td>
</tr>
<tr>
<td>HTA trial intervention</td>
<td>N C C C C C N C C C C</td>
<td>2.29</td>
<td>959</td>
<td>21.7</td>
<td>10.7</td>
<td>16.4</td>
<td>Intervention arm for proposed HTA trial</td>
</tr>
<tr>
<td>Treat groups 1-6, 8-10</td>
<td>I I I I O I N I I I N N</td>
<td>-4.5</td>
<td>1224</td>
<td>35.1</td>
<td>11.0</td>
<td>15.9</td>
<td>Optimal non-testing strategy minimising antibiotics</td>
</tr>
<tr>
<td>Treat groups 1-10</td>
<td>O I I I O I O O O I N N</td>
<td>-4.8</td>
<td>1217</td>
<td>35.2</td>
<td>17.8</td>
<td>15.6</td>
<td>On cost effectiveness frontier</td>
</tr>
<tr>
<td>Treat groups 1-10</td>
<td>I I I I O I O I I I N N</td>
<td>-4.7</td>
<td>1285</td>
<td>36.8</td>
<td>19.0</td>
<td>16.7</td>
<td>On cost effectiveness frontier</td>
</tr>
<tr>
<td>Culture test groups 7,</td>
<td>I I I I O I C I I I C C</td>
<td>-0.6</td>
<td>1836</td>
<td>46.5</td>
<td>20.7</td>
<td>27.4</td>
<td>Optimal testing strategy minimising antibiotics</td>
</tr>
<tr>
<td>11, 12; treat groups 1-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6, 8-10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture test groups 11,</td>
<td></td>
<td>-1.3</td>
<td>1870</td>
<td>48.1</td>
<td>27.7</td>
<td>27.9</td>
<td>On cost effectiveness frontier</td>
</tr>
<tr>
<td>12; treat groups 1-10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture test groups 11,</td>
<td></td>
<td>-1.1</td>
<td>1897</td>
<td>48.5</td>
<td>27.4</td>
<td>27.9</td>
<td>Maximum net benefit</td>
</tr>
<tr>
<td>12; treat groups 1-10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCR test groups 11, 12,</td>
<td></td>
<td>2.1</td>
<td>1958</td>
<td>46.8</td>
<td>27.1</td>
<td>29.1</td>
<td>On cost effectiveness frontier</td>
</tr>
<tr>
<td>treat groups 1-10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCR test groups 11, 12,</td>
<td></td>
<td>2.9</td>
<td>1965</td>
<td>46.2</td>
<td>27.1</td>
<td>29.3</td>
<td>On cost effectiveness frontier</td>
</tr>
<tr>
<td>treat groups 1-10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RCOG=Royal College of Obstetricians and Gynaecologists; HTA=Health Technology Assessment; N=No intervention; ITreat with intravenous penicillin without testing; CTreat with culture at 35-37 weeks, and treat positive cases with intravenous penicillin; ONtreat with oral erythromycin without testing; P=Test by polymerase chain reaction, and treat positive cases with intravenous penicillin.

*Calculated assuming 680000 deliveries annually and a ‘willingness to pay’ threshold of £25000 per QALY. Net benefit is equal to the QALYs gained multiplied by threshold value (£25000) minus the costs of the strategy.

†Stillbirths and live births with early or late onset infection.
WHAT IS ALREADY KNOWN ON THIS TOPIC

Prenatal screening for maternal group B streptococcal infection results in antibiotic treatment for 30-50% of women giving birth in the US. Such screening is not recommended in the UK because evidence is lacking about its effectiveness.

WHAT THIS STUDY ADDS

Current best practice is not cost effective, and immediate extension of routine antibiotic treatment practice to all preterm and high risk term deliveries would be beneficial and could be readily implemented. Thereafter, it is uncertain whether the optimal choice would be culture based testing for low risk women, or vaccination plus treatment of all preterm and high risk term deliveries and no testing for low risk women. Further research could be cost effective: trials to evaluate vaccine efficacy should be a priority, and trials to evaluate testing versus no intervention in low risk women could be worth while. However, the proposed £1.2m HTA trial of screening versus current best practice would randomise women to intervention and control groups that are not cost effective.

infection. There would also be value in further information comparing culture testing with PCR testing and no treatment, but only in low risk women delivering at term. Neither of these questions will be addressed by the proposed HTA trial of culture testing versus current best practice, as the comparison will be based on aggregate rates of infection in each NHS trust without separately identifying low risk women. In addition, the study raises ethical concerns about randomising 540000 women to intervention and control arms that are clearly not clinically or cost effective (fig 2).

Conclusions

Current recommendations for prepartum antibiotic use in the UK should be urgently reappraised with a view to extending treatment to all preterm and high risk term groups. Although our analysis was from a UK perspective, our results have implications for other settings where early onset infections due to pathogens other than group B streptococci predominate. In particular, policy makers should reconsider the value of testing high risk groups for maternal colonisation with group B streptococcal infection, as, given the risk of infection from pathogens other than group B streptococci and the insensitivity of screening, such women may be better off treated regardless of the test result. Research aimed at the realisation of a vaccine for group B streptococcal infection should be a priority.

We thank the following contributors to this project: Mark Sculpher and Khaliq Khan helped design the study; Carol Baker, Jim Gray, David Isaacs, Sara Kenyon, Mike Milar, and Dierdre Murphy were expert advisers; Mark Little, Phil Steer, Paul Heath, Sam Oddie, Nick Embleton, Georgia Duckworth, Catherine Goodall, Dominique Acolet, Mike Milar, San Harding, Paul Ostro, Helen Bedford, Sue Halket, and John De Louvou contributed primary datasets.

Contributors: REG, AEA, and KC conceived the study. TEC and REG carried out the systematic reviews. KC, CA, LB, and ZP undertook the economic analyses. CA, AEA, and NIW carried out the evidence synthesis analyses. REG, TEC, KC, and AEA drafted the initial report, which was commented on by all authors. REG coordinated the study and is the guarantor.

Funding: The study was funded by the UK Department of Health through its Health Technology Assessment Programme. The opinions and conclusions expressed here are those of the authors and do not necessarily reflect those of the UK National Health Service or the Department of Health.

Competing interests: None declared.
Effectiveness and safety of chest pain assessment to prevent emergency admissions: ESCAPE cluster randomised trial

Steve Goodacre, professor of emergency medicine,1 Elizabeth Cross, research associate,1 Cath Lewis, research associate,2 Jon Nicholl, professor of health services research,1 Simon Capewell, professor of epidemiology,2 for the ESCAPE Research Team

ABSTRACT

Objective To determine whether introducing chest pain unit care reduces emergency admissions without increasing reattendances and admissions over the next 30 days.

Design Cluster randomised before and after intervention trial.

Setting 14 diverse acute hospitals in the United Kingdom.

Participants Patients attending the emergency department with acute chest pain during the year before and the year after the intervention started.

Intervention Establishment of chest pain unit care compared with continuation of routine care.

Main outcome measures Proportion of chest pain department attendances resulting in admission; reattendances and admissions over the next 30 days; daily emergency department attendances (all causes); and proportion of emergency department attendances with chest pain.

Results The introduction of chest pain unit care was associated with weak evidence of an increase in emergency department attendances with chest pain (16% v 3.5%; P=0.08); no change in the proportion of chest pain attendances resulting in admission (odds ratio 0.998, 95% confidence interval 0.940 to 1.059; P=0.945); small increases in the proportion reattending (odds ratio 1.10, 1.00 to 1.21; P=0.036) or being admitted (1.30, 0.97 to 1.74; P=0.083) over the next 30 days; and evidence of increased daily medical admissions (1.7 per day, 95% confidence interval 0.8 to 2.5; P=0.001). However, this last finding was highly sensitive to changes in the method used to handle missing data.

Conclusion The introduction of chest pain unit care did not reduce the proportion of patients with chest pain admitted and may have been associated with increased emergency department attendances with chest pain.

Trial registration Current Controlled Trials ISRCTN55318418.

INTRODUCTION

Rising numbers of emergency medical admissions have caused concerns for more than a decade.1 Acute chest pain is responsible for approximately 700 000 emergency department attendances a year in England and Wales and for around a quarter of all emergency medical admissions.2 The NHS Institute for Innovation and Improvement has ranked chest pain as the number one clinical scenario by volume of admissions with potential for outpatient management and estimated that 30-60% of patients admitted with chest pain could be treated outside hospital.3

Chest pain units have been developed to reduce admissions and improve care by providing rapid and accurate diagnostic assessment for acute coronary syndrome with a short period of observation and testing of biochemical cardiac markers, followed by an exercise treadmill test.4-6 A previous trial that randomised days of the week at a single hospital to chest pain unit care or routine care showed that chest pain unit care reduced admissions by 17% among selected low risk patients, with non-significant decreases in discharges with acute coronary syndrome (14% v 6%).7

We aimed to determine whether introducing a chest pain unit, or the elements of care provided by such a unit, at a variety of hospitals would reduce the proportion of emergency department attendances with chest pain resulting in admission, without increasing reattendances and admissions over the next 30 days.

METHODS

We planned to randomise 18 hospitals to either establish chest pain unit care or continue providing routine care and then to measure outcomes before and after the intervention to determine the effect of chest pain unit care compared with routine care, adjusting for baseline differences between the two groups of hospitals. Eligible hospitals had to be able to establish chest pain unit care, not currently provide the key elements of such care, and be willing to allow the intervention to be determined by random allocation.

Intervention

On recruitment, hospitals had to set a date on which they would establish chest pain unit care if randomised to do so. This date would also act as a notional intervention date at control hospitals for determining pre-

INFORMATION FOR CONTRIBUTORS

ABSTRACT

Objective: To determine whether introducing chest pain unit care reduces emergency admissions without increasing reattendances and admissions over the next 30 days.

Design: Cluster randomised before and after intervention trial.

Setting: 14 diverse acute hospitals in the United Kingdom.

Participants: Patients attending the emergency department with acute chest pain during the year before and the year after the intervention started.

Intervention: Establishment of chest pain unit care compared with continuation of routine care.

Main outcome measures: Proportion of chest pain department attendances resulting in admission; reattendances and admissions over the next 30 days; daily emergency department attendances (all causes); and proportion of emergency department attendances with chest pain.

Results: The introduction of chest pain unit care was associated with weak evidence of an increase in emergency department attendances with chest pain (16% v 3.5%; P=0.08); no change in the proportion of chest pain attendances resulting in admission (odds ratio 0.998, 95% confidence interval 0.940 to 1.059; P=0.945); small increases in the proportion reattending (odds ratio 1.10, 1.00 to 1.21; P=0.036) or being admitted (1.30, 0.97 to 1.74; P=0.083) over the next 30 days; and evidence of increased daily medical admissions (1.7 per day, 95% confidence interval 0.8 to 2.5; P=0.001). However, this last finding was highly sensitive to changes in the method used to handle missing data.

Conclusion: The introduction of chest pain unit care did not reduce the proportion of patients with chest pain admitted and may have been associated with increased emergency department attendances with chest pain.

Trial registration: Current Controlled Trials ISRCTN55318418.

INTRODUCTION

Rising numbers of emergency medical admissions have caused concerns for more than a decade.1 Acute chest pain is responsible for approximately 700 000 emergency department attendances a year in England and Wales and for around a quarter of all emergency medical admissions.2 The NHS Institute for Innovation and Improvement has ranked chest pain as the number one clinical scenario by volume of admissions with potential for outpatient management and estimated that 30-60% of patients admitted with chest pain could be treated outside hospital.3

Chest pain units have been developed to reduce admissions and improve care by providing rapid and accurate diagnostic assessment for acute coronary syndrome with a short period of observation and testing of biochemical cardiac markers, followed by an exercise treadmill test.4-6 A previous trial that randomised days of the week at a single hospital to chest pain unit care or routine care showed that chest pain unit care reduced admissions by 17% among selected low risk patients, with non-significant decreases in discharges with acute coronary syndrome (14% v 6%).7

We aimed to determine whether introducing a chest pain unit, or the elements of care provided by such a unit, at a variety of hospitals would reduce the proportion of emergency department attendances with chest pain resulting in admission, without increasing reattendances and admissions over the next 30 days.

METHODS

We planned to randomise 18 hospitals to either establish chest pain unit care or continue providing routine care and then to measure outcomes before and after the intervention to determine the effect of chest pain unit care compared with routine care, adjusting for baseline differences between the two groups of hospitals. Eligible hospitals had to be able to establish chest pain unit care, not currently provide the key elements of such care, and be willing to allow the intervention to be determined by random allocation.

Intervention

On recruitment, hospitals had to set a date on which they would establish chest pain unit care if randomised to do so. This date would also act as a notional intervention date at control hospitals for determining pre-
intervention and post-intervention time periods. An independent researcher randomised hospitals in pairs, as soon as two consecutive hospitals were recruited (one to establish chest pain unit care and one to continue routine care).

The hospital led the process of establishing chest pain units, supported by two members of the research team. The hospital met initial set-up costs, but the Department of Health provided £106 reimbursement of costs for each patient recorded as receiving the full chest pain unit protocol. The chest pain unit protocol was applied to selected patients with no definite evidence of acute coronary syndrome or alternative pathology. The protocol consisted of two to six hours of observation and biochemical testing (creatine kinase MB [mass] on arrival and at least two hours later and troponin at least six hours after worst pain) followed by an exercise treadmill test. We ideally expected the chest pain unit to be based in or adjacent to the emergency department, staffed by specialist chest pain nurses, using laboratory biochemical tests with a rapid turnaround time and providing immediate treadmill testing in the emergency department. However, to allow care to be set up in a variety of settings, we accepted that the chest pain unit could be based on an admissions ward, cross covered by non-specialist staff, could use point of care biochemical tests, and could allow discharge home between biochemical tests and a treadmill test on the next working day based in the cardiology department.

Hospitals allocated to continue with routine care were asked to not set up a chest pain unit or introduce any of the specific elements of this care, such as short stay observation with biochemical testing or rapid exercise treadmill testing. However, they were free to continue with development of normal services, such as interventions to improve thrombolysis times and staff development.

To avoid interfering with provision of health care we used routine data sources to measure outcomes. We retrospectively identified all adult patients recorded at reception as presenting with chest pain or a related complaint (such as angina or suspected heart attack) during the year before and the year after the intervention began and then identified repeat attendances by the same person in each year. For each attendance, we recorded whether it resulted in admission or discharge. The primary outcome was the proportion of attendances resulting in admission. For each patient, we recorded whether their first attendance was followed by reattendance at the emergency department within 30 days and whether reattendance resulted in admission. We also asked each hospital to provide details of the daily number of emergency medical admissions over the study period.

Analysis
We used a random effects multilevel model to estimate the effect of chest pain unit care, compared with routine care, on each outcome in the post-intervention year, adjusting for pre-intervention differences between the two groups of hospitals. We included the hospital attended as a random effect and age, sex, hospital allocation (chest pain unit or control), and time (before or after intervention) as covariates. We made the decision to use age and sex as covariates a priori. We did the analysis on an intention to treat basis, coding attendances or patients according to the initial allocation of the hospital, regardless of whether patients actually received chest pain unit care. We used a nested analysis of variance in the logits of the proportions to test the hypothesis that the change in the proportion of attendances resulting in admission was due to the intervention.

Table 1: Characteristics of recruited hospitals

<table>
<thead>
<tr>
<th>Hospital and allocation</th>
<th>Annual emergency department attendances (adults)</th>
<th>Teaching hospital?</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain unit:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>41 734</td>
<td>No</td>
<td>Industrial town</td>
</tr>
<tr>
<td>D</td>
<td>77 121</td>
<td>Yes</td>
<td>Urban</td>
</tr>
<tr>
<td>E</td>
<td>73 862</td>
<td>No</td>
<td>Urban</td>
</tr>
<tr>
<td>G</td>
<td>37 189</td>
<td>No</td>
<td>County town</td>
</tr>
<tr>
<td>J</td>
<td>54 449</td>
<td>No</td>
<td>Industrial town</td>
</tr>
<tr>
<td>L</td>
<td>20 884</td>
<td>No</td>
<td>Rural</td>
</tr>
<tr>
<td>N</td>
<td>43 875</td>
<td>No</td>
<td>County town</td>
</tr>
<tr>
<td>Control:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>42 102</td>
<td>No</td>
<td>Industrial town</td>
</tr>
<tr>
<td>C</td>
<td>53 516</td>
<td>No</td>
<td>Industrial town</td>
</tr>
<tr>
<td>F</td>
<td>94 470</td>
<td>Yes</td>
<td>Urban</td>
</tr>
<tr>
<td>H</td>
<td>55 786</td>
<td>Yes</td>
<td>Urban</td>
</tr>
<tr>
<td>I</td>
<td>38 898</td>
<td>No</td>
<td>Industrial town</td>
</tr>
<tr>
<td>K</td>
<td>23 550</td>
<td>No</td>
<td>Industrial town</td>
</tr>
<tr>
<td>M</td>
<td>113 878</td>
<td>Yes</td>
<td>Urban</td>
</tr>
</tbody>
</table>

Table 2: Proportion of adults attending emergency department with chest pain

<table>
<thead>
<tr>
<th>Hospital and allocation</th>
<th>% with chest pain (No with chest pain/all attendances)</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain unit:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>5.8 (2409/41 734)</td>
<td>5.5 (2410/43 897)</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>6.2 (4815/77 121)</td>
<td>7.7 (6423/83 402)</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>7.0 (5134/73 862)</td>
<td>7.7 (5803/75 588)</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>5.1 (1907/37 189)</td>
<td>5.8 (2312/39 708)</td>
<td></td>
</tr>
<tr>
<td>J</td>
<td>4.6 (2511/54 449)</td>
<td>5.1 (2992/58 101)</td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>7.1 (1492/20 884)</td>
<td>6.6 (1460/22 196)</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>5.7 (2516/43 875)</td>
<td>5.8 (2701/46 471)</td>
<td></td>
</tr>
<tr>
<td>Control:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B*</td>
<td>5.5 (1643/29 873)</td>
<td>5.3 (2005/37 830)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>4.2 (2237/53 516)</td>
<td>4.5 (2334/52 224)</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>4.9 (4638/94 470)</td>
<td>4.9 (4644/94 985)</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>9.1 (5095/55 786)</td>
<td>9.1 (5368/59 232)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>4.9 (1918/38 898)</td>
<td>5.3 (2209/41 769)</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>6.8 (1596/23 550)</td>
<td>6.4 (1386/21 692)</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>5.0 (5731/113 878)</td>
<td>4.9 (5720/117 265)</td>
<td></td>
</tr>
</tbody>
</table>

*Data available for only 10 months of each year.
emergency department attendances with chest pain differed between chest pain unit and control hospitals.

We anticipated that each hospital would see approximately 4200 attendances a year with chest pain or a related complaint. Using standard sample size calculations, we estimated that 890 attendances in each hospital before the intervention and 890 after the intervention would provide 80% power to detect an absolute difference of 5% in the proportion resulting in admission ($\alpha = 0.05$). We therefore allowed for potential clustering in the primary outcome with a design effect of up to four.

RESULTS

Of the 82 hospitals that expressed an interest in participating in the trial, 11 decided to set up a chest pain unit outside the trial, 17 decided that they would not be able to set up a unit if randomised to do so, two raised concerns about research aspects of the trial, and 36 gave either other reasons or no specific reason for declining to participate. We therefore recruited 14 hospitals between October 2004 and June 2005. Table 1 outlines the characteristics of these hospitals. Control hospitals tended to be slightly larger and more urban. All seven hospitals randomised to the intervention group successfully set up a chest pain unit that remained operational for the whole year of the trial. The characteristics of these units have been detailed in a previous paper. The units varied in location, staffing, opening hours (from 9 am to 5 pm weekdays only to 24 hours a day seven days a week), and patient throughput. All hospitals provided complete data, except that hospital F was able to provide emergency medical admissions data for only 75 days before and after the intervention and hospital I could not break down admissions by route.

Overall, 37 319 patients made 43 642 attendances with chest pain in the pre-intervention year, and 40 951 patients made 47 767 attendances in the post-intervention year. Mean age was 54.2 (range 16-105) years; 32 520 (41.3%) patients were female, sex was not recorded for 4094 (5.3%) patients. Patients attending intervention hospitals were slightly older (55.5 years vs 52.8 for control), but similar proportions were male (55.8% vs 56.5%). Table 2 shows the number of chest pain related emergency department attendances at each hospital. Chest pain related attendances increased by 3.5% at control hospitals (from 22 858 to 23 666) and by 16.0% at intervention hospitals (from 20 784 to 24 101), compared with increases in all adult attendances of 2.4% at control hospitals (from 422 200 to 432 319) and 5.8% at intervention hospitals (from 349 113 to 369 363).

The figure shows the change in the percentage of total emergency department attendances presenting with chest pain for each hospital. We found some weak evidence ($P=0.08$) that the proportion of attendances with chest pain had increased more at
intervention hospitals than at control hospitals. However, this was not a consistent finding across all intervention hospitals.

Table 3 shows the proportion of chest pain attendances admitted at each participating hospital. Overall, this proportion increased at control hospitals from 52.2% \( (11 664/22 358) \) to 52.6% \( (12 255/23 278) \) but decreased at intervention hospitals from 65.4% \( (13 304/20 356) \) to 64.4% \( (15 199/23 592) \). Although chest pain unit care seemed to be associated with a small decrease in the odds of admission (unadjusted odds ratio 0.942, 95% confidence interval 0.892 to 0.994; \( P = 0.029 \)), the inclusion of age and sex in the analysis (as planned a priori) produced a non-significant result [adjusted odds ratio 0.998, 0.940 to 1.059; \( P = 0.945 \)].

Table 4 shows the proportion of patients reattending and the proportion admitted over the 30 days after initial attendance. Chest pain unit care was associated with some evidence of small increases in reattendance (unadjusted odds ratio 1.10, 1.00 to 1.21; \( P = 0.044 \)) and admission at reattendance (1.28, 0.95 to 1.72; \( P = 0.101 \)). Inclusion of age and sex as covariates did not alter these findings (adjusted odds ratio 1.10, 1.00 to 1.21; \( P = 0.036 \) for reattendance and 1.30, 0.97 to 1.74; \( P = 0.083 \) for admission).

Mean daily emergency medical admissions (all), those through the emergency department, and those through other routes were 36.1, 21.5, and 14.6 in the pre-intervention year and 37.8, 23.7, and 14.1 in the post-intervention year. At control hospitals, these values were 29.6, 20.6, and 10.5 in the pre-intervention year and 29.7, 21.8, and 9.4 in the post-intervention year. The sum of emergency department and other values does not equal the total value for the control hospitals because hospital I could not identify the route of admission. Table 5 shows these data for the individual hospitals. Availability of a chest pain unit was associated with a mean increase in all admissions of 1.7 (95% confidence interval 0.8 to 2.5; \( P<0.001 \)) a day, in emergency department admissions of 1.0 (0.4 to 1.5; \( P=0.001 \)) a day, and admissions through other routes of 0.6 (−0.1 to 1.3; \( P=0.078 \)) a day.

However, these findings are sensitive to changes in the way missing data from hospital F are handled. Exclusion of all data from hospital F changed the estimated effect of chest pain unit care on all admissions and those through the emergency department to increases of 2.0 (1.3 to 2.8) and 1.4 (0.9 to 1.9) admissions a day, whereas weighting data from hospital F so that they carry equal weight to other hospitals changed these estimates to an increase of 0.4 (−0.5 to 1.2) for all admissions.

### Table 4 | Reattendances and admissions over 30 days after initial attendance

<table>
<thead>
<tr>
<th>Hospital and allocation</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total patients</td>
<td>Reattendances (% of total)</td>
</tr>
<tr>
<td>Chest pain unit:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>2026</td>
<td>205 (10.1)</td>
</tr>
<tr>
<td>D</td>
<td>4097</td>
<td>468 (11.4)</td>
</tr>
<tr>
<td>E</td>
<td>4365</td>
<td>499 (11.4)</td>
</tr>
<tr>
<td>G</td>
<td>1656</td>
<td>135 (8.2)</td>
</tr>
<tr>
<td>J</td>
<td>2216</td>
<td>218 (9.8)</td>
</tr>
<tr>
<td>L</td>
<td>1206</td>
<td>103 (8.5)</td>
</tr>
<tr>
<td>N</td>
<td>2223</td>
<td>158 (7.1)</td>
</tr>
<tr>
<td>Control:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>1421</td>
<td>133 (9.4)</td>
</tr>
<tr>
<td>C</td>
<td>1889</td>
<td>215 (11.4)</td>
</tr>
<tr>
<td>F</td>
<td>3872</td>
<td>426 (11.0)</td>
</tr>
<tr>
<td>H</td>
<td>4335</td>
<td>420 (9.7)</td>
</tr>
<tr>
<td>I</td>
<td>1711</td>
<td>157 (9.2)</td>
</tr>
<tr>
<td>K</td>
<td>1394</td>
<td>117 (8.4)</td>
</tr>
<tr>
<td>M</td>
<td>4908</td>
<td>621 (12.7)</td>
</tr>
</tbody>
</table>

### Table 5 | Mean number of daily emergency medical admissions at each hospital

<table>
<thead>
<tr>
<th>Hospital and allocation</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Through emergency department</td>
<td>Through other routes</td>
</tr>
<tr>
<td>Chest pain unit:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>38.5</td>
<td>22.2</td>
</tr>
<tr>
<td>D</td>
<td>44.9</td>
<td>41.4</td>
</tr>
<tr>
<td>E</td>
<td>45.4</td>
<td>34.0</td>
</tr>
<tr>
<td>G</td>
<td>48.4</td>
<td>11.8</td>
</tr>
<tr>
<td>J</td>
<td>24.1</td>
<td>18.3</td>
</tr>
<tr>
<td>L</td>
<td>19.7</td>
<td>9.3</td>
</tr>
<tr>
<td>N</td>
<td>31.6</td>
<td>13.7</td>
</tr>
<tr>
<td>Control:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>30.8</td>
<td>11.8</td>
</tr>
<tr>
<td>C</td>
<td>22.4</td>
<td>17.1</td>
</tr>
<tr>
<td>F</td>
<td>85.3</td>
<td>57.0</td>
</tr>
<tr>
<td>H</td>
<td>35.4</td>
<td>29.1</td>
</tr>
<tr>
<td>I*</td>
<td>21.8</td>
<td>–</td>
</tr>
<tr>
<td>K</td>
<td>17.5</td>
<td>6.3</td>
</tr>
<tr>
<td>M</td>
<td>38.2</td>
<td>31.2</td>
</tr>
</tbody>
</table>

*Admissions not broken down by route.
Implementation of chest pain unit care does not reduce the proportion of patients with chest pain admitted and may be associated with increased emergency department attendances with chest pain.

Chest pain unit care may lead to an overall increase in emergency medical admissions and a decrease of 0.5 (−0.1 to 1.1) a day for emergency department admissions. The estimated effect of chest pain unit care on admissions through other routes was unaffected.

**DISCUSSION**

Our multicentre study is the first to compare the effect of implementing chest pain units with that of continuing routine practice at a “whole system” level across a variety of hospitals. It provides the most reliable estimate of the effect of widespread implementation of chest pain units on hospital admissions. Implementation of chest pain unit care across diverse hospitals did not reduce the proportion of attendances with chest pain admitted to hospital. Furthermore, it may have been associated with increased emergency department attendances with chest pain and overall emergency hospital admissions.

This conflicts with previous studies showing that chest pain unit care was associated with decreased admissions with chest pain.7-9,11 However, these studies either compared chest pain unit care with historical practice without a concurrent control group or evaluated the effect of chest pain unit care on the selected low risk patients who are most likely to benefit.7-9,11 The first approach carries the risk of bias from differential patient selection or confounding by concurrent changes in practice, whereas the latter may reliably show benefit in selected groups but miss knock-on effects on the wider population.

New services aimed at reducing the need for hospital care may increase demand for services and thus not reduce overall admissions,12 although there are few robust data showing this phenomenon. One recent example evaluated care management of elderly people by using a controlled, before and after design and measured emergency admission rates at practice level.13 This showed that care management introduced an additional range of services into primary care without an associated reduction in hospital admissions and concluded that this may have been because of identification of additional cases.

Although service level evaluation provides the best way of estimating effects on the whole service, it has several limitations that could lead to an erroneous conclusion that chest pain unit care is ineffective. We were unable to institute detailed follow-up to identify whether chest pain unit care led to more appropriate admission of patients with acute coronary syndrome or whether patients benefited from admission. We cannot therefore draw conclusions about the value of a potential increase in admissions. Most patients with chest pain do not receive chest pain unit care, so beneficial effects may be “diluted” in the study population. The structure, processes, and activity of the chest pain units,8 and outcomes at individual hospitals, varied substantially, so drawing conclusions about a general effect of chest pain units may be inappropriate.

**Conclusions**

The limitations outlined above mean that we cannot exclude the possibility that individual chest pain units had beneficial effects in selected groups of patients. However, we can reasonably conclude that setting up chest pain unit care throughout the National Health Service would not reduce, and could paradoxically increase, emergency medical admissions.

We thank Margaret Jane and Sarah Lampard for clinical assistance and the staff at the participating hospitals for their help with this study.

**Contributors:** SG, JN, and SC conceived and designed the study; EC and CL collected the data; SG and JN analysed the data. All authors contributed to writing the article and approved the final draft. SG is guarantor.

Principal trial staff: University Hospital Aintree (clinical manager); Simon Capewell, professor of clinical epidemiology, University of Liverpool (northwest lead); Liz Cross, research associate, University of Sheffield (research manager); Steve Goodacre, professor of emergency medicine, University of Sheffield (principal investigator); Maxine Johnson, research associate, University of Sheffield (qualitative researcher); Cath Lewis, research associate, University of Liverpool (northwest coordinator); Francis Morris, consultant in emergency medicine, Northern General Hospital, Sheffield (chest pain unit adviser); Jon Nicholl, director MCRU policy research programme, University of Sheffield (statistician); Yemi Oluboyede, research associate, University of Sheffield (health economist); Susan Read, honorary research fellow, University of Sheffield (nursing adviser); Angela Tod, principal research fellow, Centre for Health and Social Care Research, Sheffield Hallam University (qualitative adviser).

Trial Steering Committee: Phil Adams, consultant cardiologist, Newcastle upon Tyne NHS Foundation Trust (co-applicant); Tim Coats, professor of emergency medicine, University of Leicester (independent member); Nicky Cullum, professor, Centre for Evidence Based Nursing, University of York (independent chair); Alasdair Gray, consultant in emergency medicine, Edinburgh Royal Infirmary (co-applicant); Eined Hirst (lay member); Jason Kendall, consultant in emergency medicine, Frenchay Hospital, Bristol (independent member); David Newby, professor of cardiology, University of Edinburgh (co-applicant); Simon Dixon, senior lecturer, University of Sheffield (health economist).

Data Monitoring Committee: Jonathan Benger, consultant in emergency medicine, Bristol Royal Infirmary, David Gray, reader in medicine and honorary consultant physician, Epidemiology and Health Services Research Unit, Queen’s Medical Centre, Nottingham; Robin Prescott, statistical adviser, Medical Statistics Unit, Public Health Sciences, University of Edinburgh.

Principal trial staff: University Hospital Aintree—John Hollingsworth (ED lead), Erwin Rodrigues (cardiology lead), Paula McCarten (cardiac specialist nurse); Whiston Hospital—David Roe (ED lead), Dave Johns (chest pain nurse); Halton General Hospital—Serge Osula (cardiology lead), Karen Randles (cardiac nurse specialist); Wythenshawe Hospital—Darren Walker (ED lead), Warrington Hospital—Steve Crowder (ED lead), Cindy Lancaster (ED nurse); West Cumberland Hospital—Charles Brett (ED lead), Guy Bickerton (ED lead); Peterborough District Hospital—Rob Russell (ED lead), Dewsbury and District...
Hospital—Dean Okereke (ED lead); Scunthorpe General Hospital—Ajay Chawla (ED lead), Julia Lindley (administration/systems manager), Julie Housham (chest pain nurse), Sarah McGugan (chest pain nurse); Queen's Medical Centre Nottingham—Frank Coffey (ED lead), Phil Miller (ED research coordinator); Taunton and Somerset Hospital—Cliff Mann (ED lead), Andrea Haffenden (chest pain nurse), Bridget Capewell (chest pain nurse); Hairmyres Hospital—John Keaney (ED lead); City Hospital Birmingham—Nigel Langford (MAU lead); Worcestershire Royal Hospital—Rose Johnson (ED lead), David Pitcher (cardiology lead), Sue Amos (chest pain nurse), Sally Baker (chest pain nurse).

Funding: The ESCAPE trial was funded by the NHS Service Delivery and Organisation R&D programme. The funders played no role in developing the study design, in the collection, analysis, and interpretation of data, in the writing of the report, or in the decision to submit the article for publication.

Competing interests: None declared.

Ethical approval: Thames Valley research ethics committee.

Provenance and peer review: Not commissioned; externally peer reviewed.

The chest pain unit protocol and data collection form are available as extras on bmj.com.


Accepted: 30 July 2007
CLINICAL REVIEW

Managing anovulatory infertility and polycystic ovary syndrome

Adam H Balen, Anthony J Rutherford

In this second overview of the current management of infertility we discuss anovulatory infertility and polycystic ovary syndrome. This syndrome (formerly known as Stein-Leventhal syndrome) is the most common hormonal disturbance in women—around one fifth of women in the United Kingdom are affected. It is also the most common reason for women not to ovulate, and the combination of being overweight and having polycystic ovary syndrome can have a profound effect on reproductive health.

Sources and selection criteria
We referred to the Cochrane database of systematic reviews, The National Institute for Health and Clinical Excellence (NICE) guidelines for the investigation and management of infertility (2004), and our knowledge of the current literature.

What is polycystic ovary syndrome?
Anovulation is the cause of infertility in about a third of couples attending infertility clinics, and polycystic ovary syndrome accounts for 90% of such cases.1 Once tests have excluded other causes of androgen excess and menstrual disturbance, the syndrome can be confirmed by the presence of two of the following criteria—biochemical or clinical hyperandrogenism (hirsutism, acne, or alopecia); menstrual irregularity; and polycystic ovaries (figure).2 Symptoms, signs, and biochemical features vary greatly among affected women and may change over time in individual women.3 This review will concentrate on the management of infertility. The general practitioner should be able to start investigations and formulate a diagnosis before referral to a specialist in reproductive medicine.

The endocrine abnormalities in women with polycystic ovary syndrome include raised concentrations of luteinising hormone (LH; seen in about 40% of women), testosterone, and androstenedione, in association with low or normal concentrations of follicle stimulating hormone (FSH). Androgen production from the polycystic ovary is driven predominantly by luteinising hormone in slim women and insulin in overweight women. The definition of polycystic ovary syndrome recognises obesity as an association and not a diagnostic criterion. Only 40-50% of women with the syndrome are overweight.1,3

Insulin resistance is a key pathophysiological abnormality, and women with polycystic ovary syndrome have increased risk of impaired glucose tolerance, type 2 diabetes mellitus, and the metabolic syndrome. The longer the interval between menstrual bleeds the greater the degree of insulin resistance.4 Although women with polycystic ovaries are more insulin resistant than weight matched women with normal ovaries, insulin resistance is seen in only 10-15% of slim and 20-40% of obese women with the syndrome.4

The prevalence of polycystic ovary syndrome in the general population depends on the diagnostic criteria used. In the past, using the National Institutes for Health consensus5 the definition was more exclusive and population estimates were about 7%.8 Using the more recent Rotterdam consensus2 the prevalence is estimated to be as high as 20-25% in white women in the UK,7 although symptoms are often mild. The highest reported prevalence was 52% in South Asian immigrants in the United Kingdom, of whom 49% had menstrual irregularity.8 Not all women with polycystic ovaries have the clinical and biochemical features that define the syndrome, and about 20% of women with polycystic ovaries have no symptoms. Women from South Asia living in the UK have symptoms at an earlier age than their white counterparts; they also have greater insulin resistance and more severe symptoms.9

How does obesity interact with polycystic ovary syndrome?
Obesity has a profound effect on both natural and assisted conception—it influences the chance of becoming pregnant and the likelihood of a healthy pregnancy.10 Obesity is associated with increased rates of congenital anomalies (neural tube defects and cardiac defects), miscarriage, gestational diabetes, hypertension, problems during delivery, stillbirth, and maternal mortality.11 Of the 261 deaths reported between 2000 and 2002 to the UK Confidential Enquiry into Maternal Health, 78 women (35%) were obese, compared with 23% of women in the general population, and of these more than a quarter had a body mass index (BMI) >35.11

Should obese women with polycystic ovary syndrome lose weight before treatment or should they
receive treatment irrespective of the possible outcome? Several studies show that weight loss improves the endocrine profile and reproductive outcome in women with polycystic ovary syndrome. Even losing 5-10% of total body weight can reduce central fat by up to 30%, improve insulin sensitivity, and restore ovulation. Lifestyle modification is a key component of improving reproductive function in overweight anovulatory women with the syndrome. Treatment is harder to monitor in obese women as it is difficult to see the number of developing follicles in the ovaries; this increases the risk of multiple ovulation and multiple pregnancy. UK guidelines for the management of overweight women with polycystic ovary syndrome advise weight loss, preferably to a BMI of <30, to 30%, improve insulin sensitivity, and restore ovulation. Lifestyle modification is a key component of improving reproductive function in overweight anovulatory women with the syndrome. Treatment is harder to monitor in obese women as it is difficult to see the number of developing follicles in the ovaries; this increases the risk of multiple ovulation and multiple pregnancy. UK guidelines for the management of overweight women with polycystic ovary syndrome advise weight loss, preferably to a BMI of <30, to improve insulin sensitivity, and restore ovulation. Lifestyle modification is a key component of improving reproductive function in overweight anovulatory women with the syndrome.

How do we help women with the syndrome to ovulate?
Anovulatory infertility in polycystic ovary syndrome has traditionally been managed with clomifene citrate and then gonadotrophins or laparoscopic ovarian surgery in women who are resistant to clomifene. There has been a shift away from inducing ovulation of just one follicle to in vitro fertilisation—this is based on the false premise that in vitro fertilisation has greater cumulative rates of conception. Supervolulation for in vitro fertilisation is risky in women with polycystic ovaries because of the potentially life threatening complication of ovarian hyperstimulation syndrome (although this complication can occur rarely after standard induction of ovulation). Carefully conducted induction of ovulation achieves good cumulative rates of conception, and rates of multiple pregnancy can be minimised by strict adherence to criteria that limit the number of follicles that develop.

Does metformin have a role in fertility treatment?
Insulin sensitising agents, such as metformin, have been investigated because of the association between hyperinsulinaemia and polycystic ovary syndrome. Most studies included in the first systematic reviews had a small sample size and did not include a power calculation for the proposed effect. These reviews suggested that metformin—when used alone and compared with placebo—significantly lowered serum androgen concentrations and restored menstrual cyclicity. One of these early meta-analyses indicated that metformin can achieve ovulation either alone or when combined with clomifene. The meta-analysis was based on small controlled trials (not all of them double blinded), three of which came from the same centre. This illustrates the important point that meta-analysis is no substitute for adequately powered, well conducted randomised controlled trials.

Metformin seems to be less effective in significantly obese women (BMI >35). The largest appropriately powered, prospective, randomised, double blind, placebo controlled study set out to evaluate the combined effects of lifestyle modification and metformin in obese anovulatory women with polycystic ovary syndrome and a mean BMI of 38. All women were individually assessed by a dietitian to set a realistic goal that could be sustained, with an average reduction in energy intake of 2.09 MJ (500 kcal) a day. As a result, women in both the metformin treated and placebo groups lost weight, but the amount of weight did not differ between the two groups. Menstrual cyclicity increased in women who lost weight, but again this did not differ between the two arms of the study.

A multicentre study comparing clomifene plus metformin with clomifene plus placebo found no significant differences in rates of ovulation or ongoing pregnancy. Another study randomised 676 women to three treatment arms (metformin 1000 mg twice daily plus placebo, clomifene 50 mg days three to seven of cycle plus placebo, or metformin plus clomifene). Live birth rates were 7.2% (5/208), 22.5% (47/209), and 26.8% (56/209), respectively—significantly lower in the group taking metformin only than in the other two groups. Miscarriage rates were higher in the metformin only group (40.0%, 22.6%, and 25.5%, respectively). Thus, metformin is significantly less effective than clomifene as first line treatment in anovulatory infertile women with polycystic ovary syndrome, and the addition of metformin to clomifene has no significant benefit. We therefore no longer recommend metformin in the routine management of anovulatory polycystic ovary syndrome.

What are the outcomes of the induction of ovulation?
The tried and tested oral agent clomifene remains the current treatment for anovulatory polycystic ovary syndrome. A recent meta-analysis confirmed that clomifene increased pregnancy rates compared with placebo as first line therapy (fixed odds ratio 5.8, 95% confidence interval 1.6 to 21.5; number needed to treat 5.9, 3.6 to 10.7). None the less, clomifene is associated with an 11% risk of multiple pregnancy, so the ovarian response should be carefully monitored with ultrasound. Such monitoring is also mandatory.
Managing anovulatory infertility and polycystic ovary syndrome

Adam H Balen, Anthony J Rutherford

In this second overview of the current management of infertility we discuss anovulatory infertility and polycystic ovary syndrome. This syndrome (formerly known as Stein-Leventhal syndrome) is the most common hormonal disturbance in women—around one fifth of women in the United Kingdom are affected. It is also the most common reason for women not to ovulate, and the combination of being overweight and having polycystic ovary syndrome can have a profound effect on reproductive health.

Sources and selection criteria
We referred to the Cochrane database of systematic reviews, The National Institute for Health and Clinical Excellence (NICE) guidelines for the investigation and management of infertility (2004), and our knowledge of the current literature.

What is polycystic ovary syndrome?
Anovulation is the cause of infertility in about a third of couples attending infertility clinics, and polycystic ovary syndrome accounts for 90% of such cases. Once tests have excluded other causes of androgen excess and menstrual disturbance, the syndrome can be confirmed by the presence of two of the following criteria—biochemical or clinical hyperandrogenism (hirsutism, acne, or alopecia); menstrual irregularity; and polycystic ovaries (figure). Symptoms, signs, and biochemical features vary greatly among affected women and may change over time in individual women. This review will concentrate on the management of infertility. The general practitioner should be able to start investigations and formulate a diagnosis before referral to a specialist in reproductive medicine.

The endocrine abnormalities in women with polycystic ovary syndrome include raised concentrations of luteinising hormone (LH; seen in about 40% of women), testosterone, and androstenedione, in association with low or normal concentrations of follicle stimulating hormone (FSH). Androgen production from the polycystic ovary is driven predominantly by luteinising hormone in slim women and insulin in overweight women. The definition of polycystic ovary syndrome recognises obesity as an association and not a diagnostic criterion. Only 40-50% of women with the syndrome are overweight. Insulin resistance is a key pathophysiological abnormality, and women with polycystic ovary syndrome have increased risk of impaired glucose tolerance, type 2 diabetes mellitus, and the metabolic syndrome. The longer the interval between menstrual bleeds the greater the degree of insulin resistance. Although women with polycystic ovaries are more insulin resistant than weight matched women with normal ovaries, insulin resistance is seen in only 10-15% of slim and 20-40% of obese women with the syndrome.

The prevalence of polycystic ovary syndrome in the general population depends on the diagnostic criteria used. In the past, using the National Institutes for Health consensus the definition was more exclusive and population estimates were about 7%. Using the more recent Rotterdam consensus the prevalence is estimated to be as high as 20-25% in white women in the UK, although symptoms are often mild. The highest reported prevalence was 52% in South Asian immigrants in the United Kingdom, of whom 49% had menstrual irregularity. Not all women with polycystic ovaries have the clinical and biochemical features that define the syndrome, and about 20% of women with polycystic ovaries have no symptoms. Women from South Asia living in the UK have symptoms at an earlier age than their white counterparts; they also have greater insulin resistance and more severe symptoms.

How does obesity interact with polycystic ovary syndrome?
Obesity has a profound effect on both natural and assisted conception—it influences the chance of becoming pregnant and the likelihood of a healthy pregnancy. Obesity is associated with increased rates of congenital anomalies (neural tube defects and cardiac defects), miscarriage, gestational diabetes, hypertension, problems during delivery, stillbirth, and maternal mortality. Of the 261 deaths reported between 2000 and 2002 to the UK Confidential Enquiry into Maternal Health, 78 women (35%) were obese, compared with 23% of women in the general population, and of these more than a quarter had a body mass index (BMI) >35.

Should obese women with polycystic ovary syndrome lose weight before treatment or should they
Hospital—Dean Okereke (ED lead), Scunthorpe General Hospital—Ajay Chawla (ED lead), Julia Lindley (administration/systems manager), Julie Housham (chest pain nurse), Sarah McGugan (chest pain nurse); Queen’s Medical Centre Nottingham—Frank Coffey (ED lead), Phil Miller (ED research coordinator); Taunton and Somerset Hospital—Cliff Marn (ED lead), Andria Haffenden (chest pain nurse), Bridget Capewell (chest pain nurse); Hairmyres Hospital—John Keaney (ED lead); City Hospital Birmingham—Nigel Langford (MAU lead); Worcestershire Royal Hospital—Rose Johnson (ED lead), David Pitcher (cardiology lead), Sue Amos (chest pain nurse), Sally Baker (chest pain nurse).

Funding: The ESCAPE trial was funded by the NHS Service Delivery and Organisation R&D programme. The funders played no role in developing the study design, in the collection, analysis, and interpretation of data, in the writing of the report, or in the decision to submit the article for publication.

Competing interests: None declared.

Ethical approval: Thames Valley research ethics committee.

Provenance and peer review: Not commissioned; externally peer reviewed.

The chest pain unit protocol and data collection form are available as extras on bmj.com.


Accepted: 30 July 2007
Why read this summary?
This article summarises the most recent guidance from the National Institute for Health and Clinical Excellence (NICE) for healthcare professionals caring for women during labour and birth. It defines the care that women who are at low risk of complications in labour at term should expect to receive, and therefore it relates to most women giving birth in the United Kingdom.

Recommendations
NICE recommendations are based on systematic reviews of the best available evidence. When minimal evidence is available, a range of consensus techniques is used to develop recommendations. In this summary, recommendations derived primarily from consensus techniques are indicated with an asterisk (*).

General principles

- Provide information with clear explanation so that women are fully involved in decision making and supported through labour. Good communication with the healthcare team is valued by women and may improve their psychological wellbeing after birth.
- Provide supportive one to one care to women in established labour and ensure they are not left alone except for short periods—women receiving one to one care throughout their labour are significantly less likely to have a caesarean section or instrumental vaginal birth, will be more satisfied, and will have a positive experience of childbirth.
- Ensure that labour and birth progress without intervention, provided that labour is progressing normally and the woman and baby are well.*

Place of birth

- Inform women that birth is generally very safe but that the available evidence on advantages and disadvantages or cost effectiveness of different places of birth is of poor quality. Current options for birth include obstetric units, midwife led units (either standalone or alongside obstetric units), or home, although availability of midwife led units may vary locally and most births take place in hospital nowadays.
- Inform women who plan to give birth at home or in a midwife led unit that these are associated with a higher likelihood of a normal birth, with less intervention, but inform them that if something goes unexpectedly seriously wrong during labour under these circumstances, the outcome for the woman and baby could be worse than in the obstetric unit, which has access to specialised care. Inform women of the likelihood of transfer locally and how long transfer is likely to take.*

Pain relief
A woman’s desire for and choice of pain relief during labour are influenced by many factors, including her expectations, the complexity of her labour, and the severity of her pain. Flexible expectations and being prepared for labour may influence her psychological wellbeing after birth, as may good communication with the healthcare team.
- Offer the option of labouring in water, as this has been shown to reduce pain and the need for regional analgesia, with no differences in adverse outcomes.
- Inform women considering epidural analgesia that it provides the most effective pain relief in labour but also carries risks (such as longer second stage and increased likelihood of instrumental birth) and implications for their labour (such as increased monitoring of both mother and baby).

Delay in labour
Provide clear definitions, referral points, and actions for the recognition and management of delay in both the first and second stages of labour.

First stage
- Delay in labour is redefined in this new guideline as “suspected” if cervical dilation...
is less than 2 cm in four hours, taking into account descent and rotation of the fetal head and the strength, duration, and frequency of contractions.*

- Delay is confirmed if progress of less than 1 cm cervical dilation is found at assessment two hours later.*
- Whenever delay is diagnosed, support and effective pain relief should be offered and the baby monitored continuously.*
- Once delay is confirmed, nulliparous women should be offered oxytocin, having been informed that this will shorten their labour and increase the frequency and strength of contractions but not influence mode of birth. Parous women should be offered oxytocin only after review by an obstetrician.
- After oxytocin is started, assessment should take place every four hours. If progress of less than 2 cm cervical dilation occurs then caesarean section should be considered.*

Second stage

- If progress is inadequate after an hour of active pushing in nulliparous women, delay should be suspected. Amniotomy should be advised at this point, together with support and analgesia or anaesthesia.*
- If progress is inadequate after two hours of active pushing in nulliparous women and one hour in parous women, delay should be diagnosed.*
- Once delay has been diagnosed, obstetric assessment and ongoing review should occur every 15-30 minutes.* Birth would be expected to take place within a total of three hours for nulliparous women and two hours for parous women.
- Instrumental birth should be undertaken only with tested, effective anaesthesia, and the choice of instrument depends on the balance of clinical circumstance and the practitioner’s experience.*

After birth

If genital trauma is identified after birth, further detailed systematic assessment should be carried out to identify accurately the extent of the trauma and ensure appropriate repair. This should include:

- Confirmation by the woman that tested effective local or regional analgesia is in place
- Visual assessment of the extent of perineal trauma (including the structures involved, the apex of the injury, and assessment of bleeding)
- A rectal examination to assess whether any damage has occurred to the external or internal anal sphincter if there is any suspicion that the perineal muscles are damaged.

Rupture of membranes before labour

The new guideline contains changes in recommendations for women at term whose membranes rupture before the onset of labour.

- Induction of labour is appropriate about 24 hours after membrane rupture to reduce the risk of serious neonatal infection from 1% to 0.5%. (Previous advice was that women should be offered a choice of immediate induction or expectant management, with the latter not exceeding 96 hours.)
- The well woman and baby do not require any investigation or prophylaxis, but both should be observed for signs of developing infection and treated if necessary.

Improving information on safety around place of birth

Including place of birth in the guideline is politically and professionally sensitive, but collecting safety data should now be a matter of priority, so that women can be more adequately informed of the advantages and disadvantages of each place of birth. To support this, the guideline recommends the collection, audit, and oversight of maternal and neonatal mortality and serious morbidity data relating to each place of birth and the development of clear pathways for referral to the obstetric unit should that be required.

These events are rare so the guideline also recommends the establishment of national surveillance of this information, which should include a national registry of all deaths resulting from events occurring during labour at term, and of neonatal encephalopathy.

Overcoming barriers

Barriers to implementation are complex and varied, and some recommendations seem more expensive than others to implement. For example, adopting the recommendation for women to labour in water may require changes in service provision if maternity units do not have sufficient baths or pools; it will also require support and possible additional training for midwives and other healthcare professionals, as well as for the women themselves. However, if maternity units are prepared to embrace change and to implement such recommendations health outcomes will improve, as will clarity and consistency of care.

NICE has developed tools to help organisations implement the guidance (see www.nice.org.uk?page.aspx?0=tools).

Contributors: All authors contributed to reviewing the evidence and writing and correcting the article. SK wrote the paper, which was commented on by the other authors.

Funding: The National Collaborating Centre for Women’s and Children’s Health was commissioned and funded by the National Institute for Health and Clinical Excellence to write this summary.

Competing interests: None declared.

Patients with cardiac chest pain should call emergency services

Will T Roberts, Adam D Timmis

The clinical problem
In acute myocardial infarction, the risk of ventricular fibrillation (and the capacity for external defibrillation or reperfusion therapy to reduce mortality) is highest in the first 12 hours after onset of symptoms. In hospital, reperfusion therapy is now given rapidly in most cases, but the time it takes the patient with chest pain to seek medical help has resisted change. This delay accounts for as much as 75% of the total delay to treatment, and in patients outside of hospital, ventricular fibrillation soon after onset of symptoms remains the primary cause of death.

Patients with cardiac chest pain should be encouraged to seek help early from emergency services, rather than through their general practitioner or helplines such as NHS Direct.

The evidence for reperfusion
A secondary analysis of registry data on 3693 patients shows that at most half of patients with suspected heart attack seek access to medical help through the emergency services. The remainder call their primary care doctor or make their own way to hospital. Yet observational studies are consistent in showing that a direct call to the emergency services as early as possible after the onset of symptoms gets the patient to a defibrillator—in hospital if not in the ambulance—more quickly than other means of accessing help. In the United Kingdom the national infarct angioplasty project (NIAP) pilot sites report that 3.1% of 1497 patients with acute S-T segment elevation myocardial infarction who were transferred by ambulance to primary angioplasty centres had ventricular tachycardia or ventricular fibrillation requiring cardioversion, and an additional 0.4% did not require cardioversion. Cardioversion was successful in all patients, and no patients died before reaching hospital.

The observational study by the atherosclerosis risk in the community (ARIC) investigators showed that among 21 119 patients with acute myocardial infarction, use of emergency medical services reduced the odds of delayed ≥4 hours) arrival at hospital by 65% (adjusted odds ratio 0.35, 95% confidence interval 0.32 to 0.38). Findings were similar in a second observational study, the global registry of acute coronary events (GRACE), where among 3693 patients with acute ST elevation myocardial infarction, use of the emergency medical services reduced the odds of delayed ≥2 hours) hospital arrival by 35% (0.65, 0.51 to 0.83). These two observational trials of 24 812 patients show that use of the emergency medical services enables earlier hospital arrival and permits earlier delivery of reperfusion therapy. Meta-analysis of 22 randomised trials of thrombolysis, with a total of 50 246 patients, shows that earlier reperfusion decreases mortality in patients with ST elevation myocardial infarction, and a prospective cohort study in 1791 primary angioplasty patients showed that shorter onset to reperfusion time is related to reduced mortality. Thus, the use of emergency services allows earlier hospital arrival and earlier delivery of reperfusion, thereby limiting myocardial damage and improving prognosis.

Barriers to change
The time it takes the patient with chest pain to seek medical help and get to hospital has scarcely declined in recent years. Behaviour can be modified by experience—patients who have had myocardial infarction arrive at hospital sooner than patients with a first myocardial infarction. However, attempts to modify patients’ behaviour through community education programmes focusing on recognising symptoms and the need to act quickly in the event of cardiac chest pain have often been disappointing. The only large randomised trial of community intervention reported no effect on delays either by patients or transport. Programmes might benefit from targeting education at those most at risk of delaying the call for help, particularly women and elderly people.

How should we change practice?
In the short term, increasing the availability of defibrillators in busy public locations should be encouraged because their use by trained people saves lives early after the onset of acute myocardial infarction. In the longer term, heightening public awareness about the need to call the emergency services as soon as possible after the onset of cardiac chest pain is likely to be the only way to reduce prehospital delay and reduce mortality in line with other reductions achieved in hospital practice.

All healthcare professionals who deal with at-risk groups should educate them about how to recognise symptoms and the need to act quickly in the event of cardiac chest pain by calling for help from emergency services, rather than consulting general practitioners or medical helplines.
 Ethicist on the ward round

PERSONAL VIEW Daniel K Sokol

Not so long ago in the BMJ I quipped that most professional medical ethicists could not distinguish their “gluteus maximus from their lateral epicondyle” and suggested that such ethicists should undergo a short clinical attachment (BMJ 2006; 333:1226).

Soon after publication, a nephrologist kindly invited me to observe a ward round at his hospital. It proved to be a puzzling experience, not because the blood gases, creatinine levels, diagnostic tests, and myriad statistics recited by a junior doctor sounded like one of Mallarmé’s incomprehensible poems, but because, as the afternoon progressed, I noticed the patient-as-person fading behind this shroud of science. I felt comfortable with my consultant, my team with their dangling stethoscopes, the all-knowing computer wheeled by the bedside, and the timid patient, dwarfed by our confident crowd. Ethics seemed a million miles away.

This absence of ethics was most puzzling of all. I spend my days thinking, teaching, and writing about medical ethics, but there, in a group of doctors and with the patient before me, the subject seemed alien. “Think,” I urged myself, “what are the ethical issues here?”

My reverie would soon be interrupted: “Urine output . . . raised creatinine levels . . . metabolic acidosis . . . abdominal x ray.”

Even in cases that I knew had obvious ethical dimensions, such as those involving futility and end-of-life decisions, I felt powerless to use ethical reasoning since I could not perceive the ethical issues with any clarity. It reminded me of a time when, intent on discovering a card magician’s method for a trick, I got so engrossed in his patter, in Sam Spade and the evil kings (a dramatic reference to the ace of spades and the four kings), that I forgot to observe the subtle movements of the conjurer’s hands and body. Magicians, like doctors, are well aware that language can disguise reality, distracting the mind from the disappointing truth ahead, be it a palmed card or a grim prognosis.

My proximity to the patient, instead of highlighting the ethical components, obscured them. The incantation of scientific jargon, the outward confidence of the consultant and his team, the austere clinical environment, and the meekness of the patient all combined to give an air of certainty from the disappointing truth ahead, be it a palmed card or a grim prognosis.

More recently, I attempted to fill the gaping holes in my medical knowledge by spending five weeks in a southern Indian hospital, observing the work of a rural surgeon. Again, I initially struggled to perceive the ethical elements. I was enthralled by the medicine, the ritual of surgery, the mesh, the corkscrew, and other instruments, the different kinds of suture material, the mattress and subcuticular stitches, the smells and sounds and techniques. But as the days went by, as I saw more surgeries, it became easier. I learnt to zoom out of the medical and focus on the social and ethical dimensions. These more uncertain, fuzzy elements of the healing endeavour began to emerge from the mass of clinical information.

As my ethical gaze slowly sharpened, I reflected on the surgeon’s kind hearted paternalism and the submissiveness of patients; the considerable influence of relatives in decision making; the prevalence of disclosures that were “economical with the truth”; the limited importance of confidentiality in this communal setting; the perfunctory nature of obtaining consent; the ethical implications of treating illiterate and medically unsophisticated patients; the financial and emotional costs of surgery to poor families; the responsibilities of sleep deprived surgeons and anaesthetists towards their patients, their colleagues, and themselves; the difference a few words of comfort can make in times of pre-operative fear; the role of humour and camaraderie in the theatre; the wisdom of using mobile phones when operating; the extreme difficulty of speaking your mind when offence may result; the proper relationship between culture and ethical norms; and many other issues that were initially as invisible to me as the card magician’s sleights.

I was not merely thinking about clinical ethics, but actually “doing ethics,” in real time with flesh-and-blood patients.

The first step to moral action is moral perception, since an ethical problem can seldom be resolved if not first spotted. For teachers of medical ethics, developing this skill in students should be a priority and the most critical place to do so is at the bedside. Saturing an orange in a lab and suturing a uterus in a casenarean section are quite different activities. The same holds true with studying ethics in the lecture hall and “doing ethics” on the wards. The aseptic first is a poor approximation of the messy second.

Daniel K Sokol is lecturer in medical ethics and law, St George’s, University of London daniel.sokol@talk21.com
The alcohol industry: taking on the public health critics

The worldwide alcohol industry is flying high. With economic growth, changes in lifestyles, and the erosion of traditional customs and mores in many developing countries, the commercial production and consumption of alcohol has been booming. New competition within the industry has seen unparalleled growth, especially in the Asia Pacific region. And the party has only just begun. Some marketing organisations predict major growth in the cognac, whisky, and other spirits niches as Chinese markets continue to expand. The one cloud on the horizon is the public health sector. The alcohol industry wants to learn and avoid the mistakes that other industries have made; thus it has examined carefully the current state of the tobacco industry, the ever tightening regulation of smoking in public places, and the falling prevalence of smoking in developed countries.

The industry has been keen to emphasise that alcohol is not a drug, that it confers benefits and pleasures, and that it should be thought of primarily as an aid to recreation and possibly as beneficial to health. The industry’s second main message is that a small number of people experience major problems, unfortunately, but the vast majority do not. What the industry fears is any control of the overall level of alcohol consumption. Public health advocates are focusing on strategies aimed at reducing the total consumption of alcohol, and the industry’s key aim is to promote overall consumption, albeit responsibly.

As part of a sophisticated public relations process the industry has established the International Centre for Alcohol Policy, which is supported by Allied Domecq, Asahi Breweries, Bacardi-Martini, the Brown-Forman Corporation, Coors Brewing Company, Diageo, Foster’s Brewing Group, Heineken, Molson Breweries, and SAB Miller. It is based in Washington, DC, and led by Marcus Grant, a former World Health Organization expert on alcohol. The industry is determined to shape the public health debate and to protect its interests. To this end the centre has sought partners in varied parts of the public health field to endorse its position.

This central stated aim of the book—one of whose editors is Marcus Grant—is to argue that population measures alone are inadequate in combating alcohol related problems. The industry has for decades conducted an intensive lobbying campaign against population based measures to reduce consumption by increasing taxation or restricting access to alcohol. The industry argues that these measures don’t suit different cultures and contexts and may not be relevant to those individuals and groups who are at risk of problems from drinking.

The book has an interesting section on the problem of illicit distilling in some developing countries, and it has a good review of the specific harms related to such activity and the problem of estimating overall levels of consumption where it exists. However, this section has virtually no mention of the growth in the commercial production of alcohol in some of these countries and doesn’t cover particular alcohol related problems in such countries or the concerns being expressed by community advocates.

The book challenges any emphasis on population measures to reduce alcohol consumption, and to this end it aims specifically at WHO’s global burden of disease project, which cites alcohol as a major contributor to mental and physical disease in developing countries. It predictably seeks to invalidate the broader public health perspective on estimating the overall burden of disease that is related to alcohol.

The book’s final section makes a sophisticated case for partnership between industry and the health sector. However, at no stage does it explore the dangers of the industry using non-governmental organisations to pursue concerns being expressed by community advocates. The book challenges any emphasis on population measures to reduce alcohol consumption, and to this end it aims specifically at WHO’s global burden of disease project, which cites alcohol as a major contributor to mental and physical disease in developing countries. It predictably seeks to invalidate the broader public health perspective on estimating the overall burden of disease that is related to alcohol.

The book’s final section makes a sophisticated case for partnership between industry and the health sector. However, at no stage does it explore the dangers of the industry using non-governmental organisations to pursue concerns being expressed by community advocates. The book challenges any emphasis on population measures to reduce alcohol consumption, and to this end it aims specifically at WHO’s global burden of disease project, which cites alcohol as a major contributor to mental and physical disease in developing countries. It predictably seeks to invalidate the broader public health perspective on estimating the overall burden of disease that is related to alcohol.

This central stated aim of the book—one of whose editors is Marcus Grant—is to argue that population measures alone are inadequate in combating alcohol related problems. The industry has for decades conducted an intensive lobbying campaign against population based measures to reduce consumption by increasing taxation or restricting access to alcohol. The industry argues that these measures don’t suit different cultures and contexts and may not be relevant to those individuals and groups who are at risk of problems from drinking.

The book has an interesting section on the problem of illicit distilling in some developing countries, and it has a good review of the specific harms related to such activity and the problem of estimating overall levels of consumption where it exists. However, this section has virtually no mention of the growth in the commercial production of alcohol in some of these countries and doesn’t cover particular alcohol related problems in such countries or the concerns being expressed by community advocates.

The book challenges any emphasis on population measures to reduce alcohol consumption, and to this end it aims specifically at WHO’s global burden of disease project, which cites alcohol as a major contributor to mental and physical disease in developing countries. It predictably seeks to invalidate the broader public health perspective on estimating the overall burden of disease that is related to alcohol.
Running with the pantomime horses

After four children a man can lose his figure. I would smile with resignation at the predictable comments: “You’re looking well!” (translation: “Aren’t you fat!”) But most days I was lucky to have time to brush my teeth, let alone fret about my body mass index or go to the gym. Anyway, the exercising class exercised me. It was demanding, unrealistic, and never satisfied with my explanation that simply resting might be sensible. The accessories were ridiculous: orthotic insoles, straps, isotonic fluids, food supplements. Jogging from one specialist physiotherapist to another, each giving an unlikely but grand sounding diagnosis and equally grand bill. Seemingly intelligent people were reduced to believing in the unscientific voodoo that much of sports medicine is.

But I took the plunge. Never underestimate the power of sibling rivalry: my brother had starting running. For 30 minutes I rumbled in the bargain buckets of sportswear websites. My finger hovered, hesitated, and then clicked. The discounted running shoes arrived the next day, and I joined the exercise bores.

At first I ran each time for 15 gut-wrenching minutes, praying that I might die. Five times a week, in the margins of the day: early morning and in the evening darkness. Dim I may be, but determined I certainly am. The time crept up, to 20, 30, and then 40 minutes. With indie rock in my earphones, the miles slipped by. I splashed through puddles, loving the rain, wind, cold, and solitude. I dodged dogs and drunken local youths, and still I plodded on.

My kids did a double act. “Dad’s gone mental obsessive,” said my daughter, and my son twirled his finger at his temple. “Bonkers, man,” they told everyone. I endured a swollen ankle and chronic hip pain, but through the pain I pounded on. One Saturday morning I sped faster and faster up a hill, with the rising sun. Trumpets blasted: I had my Rocky Balboa moment.

God, it was good to be alive.

With my previously plum shaped face now a wrinkled prune, I smile in resignation at the predictable “Are you all right? You look sick.” But exercise is an elixir of life, a treatment with a number needed to treat (NNT) of one to help prevent obesity, mood swings, cardiovascular disease, osteoporosis, and many other modern ailments. Medicine—with all its polypills, distorted risk, huge NNTs, and undebated treatment paradoxes—collapses on the starting line. So last Sunday was the Great North Run, my number 37 474—in the paddock with pantomime horses. Never mind: I am glad to be on the stage of life, not sitting in the dark watching the action, occasionally scrambling on the floor for sweets.

Des Spence is a general practitioner, Glasgow
destwo@yahoo.co.uk

A different perspective

We have peace now in Northern Ireland, which is a good thing—although it’s ironic that the deal could have been done 30 years and thousands of lives ago and was originally scuppered by the very people now in power. There is an unpleasant lesson here: in any negotiation, you need the extremists on board. They’re the ones who can make the deal stick, as no one can accuse them of selling out without losing, for example, their thumbs.

I was aware of this bitter pill when we introduced an appointment system. Appointment systems were then viewed with suspicion, undermining the right of every patient to queue, the queue being not just a line of people but something much greater: a never ending social event, the ordinary person’s forum for complaining about life in general and the health service in particular. Abolishing it was a sign that the liberal socialist elite was at its clandestine work again.

Mrs Magee turned up every day around 10 am; she considered this a human right, and waiting for more than a few minutes only further augmented her cherished sense of grievance. If you asked whether a glass was half full or half empty, she’d reply, “What’s in the glass? And by the way, I’ve an awful sore throat; I want an antibiotic. And my leg’s giving me the jip. What about an x ray?”

Mrs Magee was my Hamas, my Taliban. I knew that if she could be courted and seduced, the battle was won; if not, a mob with torches and pitchforks was just around the corner.

On the first day of the new system I processed the early patients with robotic (yet deeply empathetic) efficiency. When Mrs Magee arrived, usually as welcome a sight as blood in my stools, I was beaming at the door and tap dancing with delight.

“You are like a breath of spring, whispering of the joys to come while deep in the heart of a long yet lustrous winter, Mrs Magee,” I rhapsodised, my feelgood factor bursting out all over. “Come into my parlour, have a cup of tea, maybe a few little fruit cakes. Or what about some fresh scones hot off the griddle, and perhaps a foot massage as well?”

Mrs Magee cast a cynical eye over the vast emptiness of the waiting room and drew her own conclusion, my snark becoming a boojum.

“Not very popular, are you?” she said.

Liam Farrell is a general practitioner,
Crossmaglen, County Armagh
William.Farrell@528.gp.n-i.nhs.uk
Doctor-anarchists in class war

There is no more distinguished a writer in Britain today than J G Ballard, who was briefly a medical student but gave up to become a writer. He was born in Shanghai in 1930, but was interned in a Japanese camp there in 1943. Having previously lived the comfortable life of the rich and privileged expatriate in a poor country, he became sensitive as no one else in contemporary letters to the fragility of our well ordered existence.

Many of his books record the barbarism that lies just below the surface of our apparently civilised conduct, and that our highly technological society favours because of its tendency to isolate us emotionally from one another. Ballard is the prophet of social pathology, particularly among the educated middle classes: the vile behaviour of middle class football supporters, for example, would not surprise him in the least.

It is irrational, no doubt, but I feel some personal connection with Ballard because my grandfather, a doctor, was in Shanghai at the time that Ballard was in the camp.

Doctors figure prominently in Ballard’s fiction, as if he somewhat regretted not having become one. But the doctors of his dystopian novels do not behave better than others—far from it; and the fact that they so frequently behave badly, or at least not well, is symbolic of how fragile the author thinks that their ethical standards are, and therefore (since doctors are generally so highly regarded by the rest of society) how fragile all ethical standards are. We should not forget that many Japanese and German doctors committed some of the most sadistic atrocities of all.

Ballard’s novel, High-Rise, has several doctors as characters: a lecturer in physiology at a medical school, a psychiatrist, some neurosurgeons, and a gynaecologist. The book is typical of his dystopian genre. The high-rise of the title is one of four 40-storey apartment blocks built in the docklands area of London (as the novel was first published in 1975, the very location is an instance of Ballard’s uncanny prescience).

The residents of the new development, all of the professional classes, start a war against each other of a class nature (the higher the floor you live on, the higher your social status). Eventually there is total anarchy. Everything is vandalised, the services cease to work, garbage accumulates everywhere, the walls are covered in graffiti, and the residents raid one another for food and eat each other’s pet dogs. Almost every element of the horror is visible today, in less extreme form, and so we cannot just dismiss the author’s vision as morbid or ridiculous.

Pangbourne, the gynaecologist, is among the worst characters in the breakdown of order. Rich and successful, he lives on the highest floor, the 40th, and has led a raid with women acolytes to the lower floors, capturing “a cost-accountant from the 32nd floor with a bandaged head, and a myopic meteorologist from the 27th.” Pangbourne playfully asks what should be done with them:

“Pangbourne turned to his guests [the captured men]. ‘I rather like Flying School. Did you know we’ve been running a flying school here? No?’”

“We’ve decided to offer you some free lessons,” [acolyte] Anne Royal told them.

“One free lesson,” Pangbourne corrected. ‘But that’s all you’ll need. Isn’t it, Anne?’

“It’s a remarkably effective course.”

“Solo first time, in fact.”

Then they fix some papier mâché wings to the “guests,” preparatory to throwing them out of the window.

Which of us has never met a Pangbourne?

Theodore Dalrymple is a writer and retired doctor

---

**BETWEEN THE LINES**

**Theodore Dalrymple**

Ballard is the prophet of social pathology, particularly among the educated middle classes

---

**MEDICAL CLASSICS**

Cancer Ward By Aleksandr Solzhenitsyn

First published 1968

The semi-autobiographical novel Cancer Ward is set in a cancer hospital in the Soviet province of Uzbekistan in the late 1950s. Like Solzhenitsyn, the main character, Oleg Kostoglotov (“bone chewer”) spends some years in the Gulag, is sentenced to perpetual exile in Kazakhstan, becomes ill with cancer, is treated in a cancer clinic, and makes a good recovery. The book describes the profound effects that the experience of labour camps, exile, and then cancer can have on an individual.

Cancer Ward is meant to be understood as a political allegory—tumours kill, so how can a country survive with “growths” like labour camps and exiles? The ward, with its heterogeneous mix of patients from different ethnic groups and social backgrounds, reflects to a certain degree Soviet society. There are fierce debates on, for instance, social origin. The opportunistic apparatchik Rusanov, who has made a successful career out of denouncing friends as well as foes, prides himself on his proletarian forebears. Kostoglotov booms at him in response that even if he, Rusanov, had 10 proletarian grandfathers, if he were not a worker himself, he wouldn’t be a proletarian.

What is much less well known than the allegorical dimensions of Cancer Ward is the psychological realism of the portraits of both patients and staff. We see how being admitted to the cancer ward is like being sent to the Gulag. In both cases there may be a loss of status, loss of individuality, and loss of a future perspective. We see how cancer can isolate sufferers from even their closest relatives and friends, how some patients become anxiously preoccupied and constantly check their bodies for physical changes, how they sometimes come to think that it is no longer they but the tumour that is in charge, and how they may feel as if they were dead.

Solzhenitsyn has an equally good understanding of the mindset of the doctors. The main purpose of the ward round is to improve the morale of the patients. Euphemisms, vague formulations, and downright lies are routine tools of the trade. The doctors rarely say what they think—until they sit down together later and “the general impression of improvement and recovery was completely exploded.” One patient who has not responded to treatment is simply ignored by the doctors. Patients are discharged before they can die in order to improve the clinical statistics—no palliative care here. In individual consultations with patients some of the doctors are more honest, and even show natural kindness, rather than mere professional kindness. When Ludmila Dontsova, the lead oncologist, becomes ill with cancer, she does not want to know anything about the details of her condition, treatment, or prognosis.

Cancer Ward is not only a forceful indictment of political abuse, but an insightful and cogent study of the psychological reactions of both doctors and patients to life threatening illness.

Paul Crichton, consultant psychiatrist, London paulcrichton@doctors.org.uk
In 1952 at Blegdams Fever Hospital, Mogens Bjømboe was temporarily in charge when a baby with tetanus was admitted. Remembering his meeting with Ingrid Ibsen on the ship, he sent for Bjørn Ibsen. They jointly decided to paralyse the baby with curare to abolish the tetanus spasms and ventilate by hand. The baby did well until it was transferred to the standard regimen of controlling the spasms with sedation, when it died; but a lesson was learnt.

A few weeks afterwards, Copenhagen had one of the world’s worst polio epidemics—2899 cases in a population of 2m. Fifty or more patients a day were admitted to Blegdams Hospital. Too weak to cough, many patients drowned in their own secretions. Larssen, the chief physician, sought Ibsen’s advice. Ibsen had recently anaesthetised a patient with a tracheostomy and discovered how easy it was to intubate a patient who already had a free airway. He had learnt in Boston that inadequate ventilation caused carbon dioxide retention with hypertension and sweating, and recognised these symptoms in patients with polio. Patients were dying not from kidney failure but from carbon dioxide retention. He proposed that patients were given a tracheostomy with an airtight seal, which would keep saliva out of the lungs, which could then be cleared of secretions and ventilated with positive pressure. He proposed adding a carbon dioxide absorber and used equal parts oxygen and nitrogen in case ventilation became inadequate.

Larssen was sceptical but relented when he saw a dying 12-year-old quadriplegic girl with a collapsed lung gasping for air and drowning in her own secretions. Ibsen did an immediate tracheostomy and inserted a cuffed tube, attaching a to and fro absorption system, which gave good suction. Bronchospasm and secretions still made it impossible to reinflate the lungs. Desperate, he gave her pentothal to stop her struggling. She stopped breathing and collapsed, and he found that in this state he could inflate her lungs.

Returned to the tank ventilator, her ventilation returned and she became cyanotic. Oxygen improved her colour but her carbon dioxide continued to rise. She was taken out of the ventilator, and manual ventilation improved her again. The lesson was obvious.

Ibsen and Larssen moved patients needing ventilation to dedicated wards. Surgeons, anaesthetists (including the 20 WHO trainees), and medical and dental students were trained to aspirate secretions and perform manual ventilation in shifts of six hours. At the height of the epidemic, 70 patients were being manually ventilated. In all, 1500 students put in a total of 165 000 hours, and mortality plummeted from 80% to 25%.

Other countries took note, and the British Journal of Anaesthesia suggested that a similar scheme should be adopted in the United Kingdom. Thus began the concept of intensive therapy.

After the epidemic subsided, a Kommune hospital surgeon appointed Ibsen to organise an anaesthetic service there. A year later, in 1954, he was appointed consultant anaesthetist, in charge of his own department, with the same salary as his surgical colleagues. This gave Ibsen the financial security that enabled him to pursue his interest in intensive therapy. With the realisation that having intensive treatment facilities for different diseases was a waste of resources, the first intensive therapy unit was opened under his supervision in the Kommunehospital on 1 August 1953. It was copied around the world. His interests progressed to monitoring and, when acute medicine was moved away from the hospital in 1975, towards pain management.

Ibsen was on the editorial board of Acta Anaesthesiologica Scandinavica from its inception in 1961. He was awarded the Danish poliomyelitis medal and anaesthetic medal, and the Purkinje medal from Czechoslovakia. He was a corresponding member of the Society of Anaesthetists of Great Britain and Ireland, and was the first honorary member of the European Resuscitation Council. He wrote two textbooks on anaesthetics and intensive care in Danish (1950 and 1959), From Anaesthesiologen to Anaesthesiologen in 1965, and a memoir, Gesynsglade (“The Happiness of Reunions”), in 1990. His wife died in 1984.

Caroline Richmond
Bjørn Ibsen, anaesthetist and intensivist, Rigshospitalet, Kommunehospital, and Anaesthesiology Centre, Copenhagen (b 1915; q Copenhagen 1940), d 7 August 2007.

A full account of Ibsen’s work is given in Anesthesia and the Practice of Medicine: Historical Perspectives, by Keith Sykes and John Bunker (RSM Press 2007), to which I am indebted.

For the full versions of articles in this section see bmj.com
**Michael Gerald Askew**
Former general practitioner Gosport (b 1933; q St George’s, London, 1959; FRCPGP), died from lung cancer on 6 August 2007.

After house jobs at St George’s, Michael Askew (“Mike”) joined the navy, serving at Dartmouth College, the Dartmouth Squadron, and Royal Naval Hospital Haslar. Later he became a singlehanded practitioner, caring particularly for British and overseas naval families. His was the first practice in Gosport to computerise, and it grew to need three other partners by the time Mike retired. Mike taught a succession of young naval doctors and medical students and served on the Wessex Faculty of the Royal College of General Practitioners as treasurer and provost. He also won international prizes for photography and was president of the Southampton Photographic Club. He leaves a wife, Jackie, and three sons.

Donald McNutt
Roz Reid

---

**Nina Agnes Jane Carson**
Former senior lecturer in child health Queen’s University, Belfast (b 1923; q Queen’s University, Belfast, 1946; DM, FRCP), died from complications of cerebrovascular disease on 3 June 2007.

In 1963 Nina Carson characterised biochemically the then unknown disease of homocystinuria, her clinical and laboratory work until her retirement in 1983 contributing to its understanding and treatment. She promoted routine neonatal screening for metabolic disorders, stabilising the original test for phenylketonuria and implementing newborn blood (Guthrie) screening. She was a member of the Medical Research Council Steering Committee for Phenylketonuria to improve outcome for patients, and she helped to develop routine screening for congenital hypothyroidism in 1980. Nina was national Irish backstroke champion, and, with her husband, won Ulster and Irish sailing championships. She leaves a husband, Jim; three children; and eight grandchildren.

Dennis Carson

---

**Ian Patrick Mulligan**
Consultant cardiologist Milton Keynes General Hospital (b 1955; q St Thomas’s, London, 1979; DPhil, FRCP), died from a heart attack on 25 July 2007.

Ian Mulligan qualified with a first class intercalated degree, rapidly obtaining the MRCP. He worked in London, Northampton, Cardiff, and then Oxford, where basic research in muscle physiology led to a DPhil, followed by postdoctoral research on cardiac myocytes. As a senior registrar in Oxford, he also published a well-cited paper in the *Lancet* on the use of evidence based medicine on the acute medical take. In 1998 he was appointed to Milton Keynes Hospital, serving on many committees to establish the new cardiac annexe with a dedicated cardiac angiography facility. Ian had many interests outside work: he held a private pilot’s licence, read widely (especially history), was learning Spanish, and was an accomplished painter, a keen salsa dancer, and widely travelled. He leaves a wife, Jane, and innumerable friends.

Patrick Davey

---

**Anand Mohan Sur**
Professor of child health and consultant paediatrician Nagpur, India (b 1929; q Nagpur 1952; DCH, FRCPed, FICMH), d 26 July 2007.

Anand Sur founded the department of paediatrics at Nagpur and made paediatrics a separate subject at final MB BS level for the first time in India. He worked for some time in the United Kingdom, training at the Royal Hospital for Sick Children, Edinburgh, and Great Ormond Street Hospital, London, and becoming the youngest and first to gain the FRCPed in central India. He was an accomplished linguist, published on Indian childhood cirrhosis and childhood asthma, and was regional adviser for Western India to the Royal College of Physicians of Edinburgh until his death. He leaves a wife, Sobita, and two children.

Poorvaali Sur

---

**David Tidmarsh**
Former consultant psychiatrist Broadmoor Special Hospital, Crowthorne, Berkshire (b 1932; q Cambridge/St Bartholomew’s Hospital, London, 1958; DPM, MD, FRCPsych), died from cancer of the colon on 9 July 2007.

In 1961, after demobilisation as a prime mover in establishing a new medical school at Kilimanjaro Christian Medical Centre, pioneering a surgical training programme, including a surgical intensive care unit, in Moshi. Later he established and directed a private hospital in Arusha. An organist in his local church, he also served on management committees of the Evangelical Lutheran Church in Tanzania. He leaves a wife, Bassila, and five children.

Krishna Somers

---

**Japhet Mara Urasa**
Consultant surgeon Kilimanjaro Christian Medical Centre, Moshi, Tanzania (b 1934; q Makerere 1962; FRCS), died from a ruptured aortic aneurysm on 23 June 2007.

Japhet Mara Urasa had a major role in setting up the medical school in Dar es Salaam, combining his clinical appointment with teaching anatomy. He completed his surgical training in the United Kingdom, and on his return home worked in various regional centres. He was a prime mover in establishing a new medical school at Kilimanjaro Christian Medical Centre, pioneering a surgical training programme, including a surgical intensive care unit, in Moshi. Later he established and directed a private hospital in Arusha. An organist in his local church, he also served on management committees of the Evangelical Lutheran Church in Tanzania. He leaves a wife, Marlen, and two daughters.

Henry R Rollin
Minerva is a great supporter of disease prevention strategies, but she was taken aback to learn from an employee at the World Health Organization that WHO has adopted a policy of not employing smokers in any capacity. Advertisements for jobs apparently now include a rider that smokers “need not apply.” Doubtless it’s only a matter of time before obese people are sidelined too.

Alcohol absorption differs from person to person, and the type of “mixer” consumed with alcohol is one of the influencing factors. Volunteers participated in a study of vodka mixed with still water, carbonated water, or no mixer at all, consumed over five minutes and followed by an overnight fast. Alcohol concentrations in breath showed that 20 of the 21 participants absorbed the diluted vodka faster than the neat vodka, and that absorption was significantly quicker with a mixer of carbonated water (Journal of Forensic and Legal Medicine 2007;14:398-405).

In the absence of any obvious task, the adult brain shows spontaneous and intrinsic resting state “networks” of activity on functional magnetic resonance imaging. Little is known about the development of these networks, but new research involving functional magnetic resonance images from 12 sleeping preterm infants has found that networks are present in the infant brain (Proceedings of the National Academy of Sciences of the USA 2007 September 18, www.pnas.org/cgi/). As in adult brains, some of these networks were found in regions usually associated with movement and visual and auditory processing.

Slí-na-Sláinte (path to health), the Irish project for heart health that uses signposted walking routes, turns out to be one of those things that was probably a good idea at the time, but in reality seems to have made little difference to public health (Journal of Public Health 2007;29:222-9). The findings of a qualitative focus group study suggest that the “path to health” initiative will probably a good idea at the time, but in reality turns out to be one of those things that was probably a good idea at the time, but in reality may benefit people with haemophilia and other blood clotting disorders.

Babies who wear the wrong type of sock can develop “sock line bands” when tight bands of elastic cause inflammation in the dermis or in the subcutaneous fat. Even when healed the bands can leave visible marks. According to dermatologists, sock line bands are benign and are different from other types of raised limb bands found in babies that are not linked to clothing. These “acquired raised bands of infancy” or “amniotic band syndrome” develop in utero and are not benign (British Journal of Dermatology 2007;156:578-9).

Mice that are housed alone rather than in groups are more likely to become obese and develop diabetes, and it’s not just to do with how much they eat. Over time, the isolated mice reduced their energy expenditure and also started to eat more (Endocrinology 2007;148:4658-66). A host of complex hormonal changes are involved, but social isolation seems to be an important environmental factor in the development of obesity and diabetes.

Peter Nowell’s 1960 discovery of the Philadelphia chromosome as a hallmark of chronic myelogenous leukaemia was the first documentation of a genetic “signature” of cancer. For almost 50 years scientists have been trying to answer the questions thrown up by this discovery, but the number of questions exceeds the answers so far gleaned. What’s clear is that the Philadelphia chromosome created the paradigm for how discoveries in basic science can lead to effective treatments for human disease (Journal of Clinical Investigation 2007;117:2030-2).

Serendipity is defined as “accidental sagacity”—the sort of situation needed for discovering something you’re not consciously seeking. The discovery of penicillin is an obvious example. Today’s hectic world allows little time for pursuing serendipitous ideas, so the Dunhill Medical Trust has developed “serendipity awards.” The intention is that the awards should be used to obtain enough evidence to convince other funding bodies to take ideas forward. For more information go to www.dunhillmedical.org.uk. (In case you’re wondering, the trust says it no longer has any connection with the tobacco industry.)

A novel microscopy technique has allowed researchers to watch the creation and journey of a generation of mouse platelets. Using still imaging techniques, they’ve watched the megakaryocytes in bone marrow extending immature, proplatelet-like protrusions into microvessels. Once they are in the blood vessels, these extensions seem to be sheared from their stems by flowing blood, leading to proplatelets appearing in the peripheral bloodstream (Science 2007;317:1767-70). A better understanding of this developmental journey may benefit people with haemophilia and other blood clotting disorders.

Another example of a public health initiative that promised great things but hasn’t made much difference is described in Circulation (2007;116:1380-5). In Denmark 35 000 manikins and DVDs were distributed to schoolchildren (aged 12-14) to help teach them to perform bystander cardiopulmonary resuscitation (CPR). The children then used these to teach the technique to family and friends in a CPR learning cascade. However, the incidence of bystander CPR did not increase in the months following the project, compared with the year before.

Minerva is a great supporter of disease prevention strategies, but she was taken aback to learn from an employee at the World Health Organization that WHO has adopted a policy of not employing smokers in any capacity. Advertisements for jobs apparently now include a rider that smokers “need not apply.” Doubtless it’s only a matter of time before obese people are sidelined too.